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TABLE OF CONTENTS

ABSTRACT	1
PLAIN LANGUAGE SUMMARY	2
SUMMARY OF FINDINGS	3
BACKGROUND	8
OBJECTIVES	9
METHODS	9
RESULTS	12
Figure 1.	13
Figure 2.	15
Figure 3.	16
DISCUSSION	19
AUTHORS' CONCLUSIONS	21
ACKNOWLEDGEMENTS	22
REFERENCES	23
CHARACTERISTICS OF STUDIES	26
ADDITIONAL TABLES	39
APPENDICES	43
CONTRIBUTIONS OF AUTHORS	43
DECLARATIONS OF INTEREST	43
SOURCES OF SUPPORT	44
DIFFERENCES BETWEEN PROTOCOL AND REVIEW	44
INDEX TERMS	44

[Intervention Review]

Telerehabilitation for persons with multiple sclerosis

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ABSTRACT

Background

Telerehabilitation, an emerging method, extends rehabilitative care beyond the hospital, and facilitates multifaceted, often psychotherapeutic approaches to modern management of patients using telecommunication technology at home or in the community. Although a wide range of telerehabilitation interventions are trialed in persons with multiple sclerosis (pwMS), evidence for their effectiveness is unclear.

Objectives

To investigate the effectiveness and safety of telerehabilitation intervention in pwMS for improved patient outcomes. Specifically, this review addresses the following questions: does telerehabilitation achieve better outcomes compared with traditional face-to-face intervention; and what types of telerehabilitation interventions are effective, in which setting and influence which specific outcomes (impairment, activity limitation and participation)?

Search methods

We performed a literature search using the Cochrane Multiple Sclerosis and Rare Diseases of the Central Nervous System Review Group Specialised Register(9 July, 2014.) We handsearched the relevant journals and screened the reference lists of identified studies, and contacted authors for additional data.

Selection criteria

Randomised controlled trials (RCTs) and controlled clinical trials (CCTs) that reported telerehabilitation intervention/s in pwMS and compared them with some form of control intervention (such as lower level or different types of intervention, minimal intervention, waiting-list controls or no treatment (or usual care); interventions given in different settings) in adults with MS.

Data collection and analysis

Two review authors independently selected studies and extracted data. Three review authors assessed the methodological quality of studies using the GRADEpro software (GRADEpro 2008) for best-evidence synthesis. A meta-analysis was not possible due to marked methodological, clinical and statistical heterogeneity between included trials and between measurement tools used. Hence, we performed a best-evidence synthesis using a qualitative analysis.

Main results

Nine RCTs, one with two reports, (N = 531 participants, 469 included in analyses) investigated a variety of telerehabilitation interventions in adults with MS. The mean age of participants varied from 41 to 52 years (mean 46.5 years) and mean years since diagnosis from 7.7 to 19.0 years (mean 12.3 years). The majority of the participants were women (proportion ranging from 56% to 87%, mean 74%) and with a relapsing-remitting course of MS. These interventions were complex, with more than one rehabilitation component and included physical activity, educational, behavioural and symptom management programmes.

All studies scored 'low' on the methodological quality assessment. Overall, the review found 'low-level' evidence for telerehabilitation interventions in reducing short-term disability and symptoms such as fatigue. There was also 'low-level' evidence supporting telerehabilitation in the longer term for improved functional activities, impairments (such as fatigue, pain, insomnia); and participation measured by quality of life and psychological outcomes. There were limited data on process evaluation (participants'/therapists' satisfaction) and no data available for cost effectiveness. There were no adverse events reported as a result of telerehabilitation interventions.

Authors' conclusions

There is currently limited evidence on the efficacy of telerehabilitation in improving functional activities, fatigue and quality of life in adults with MS. A range of telerehabilitation interventions might be an alternative method of delivering services in MS populations. There is insufficient evidence to support on what types of telerehabilitation interventions are effective, and in which setting. More robust trials are needed to build evidence for the clinical and cost effectiveness of these interventions.

PLAIN LANGUAGE SUMMARY

Telerehabilitation for persons with multiple sclerosis

Review questions

Does telerehabilitation achieve better outcomes in persons with multiple sclerosis compared with traditional face-to-face intervention? What types of telerehabilitation interventions are effective, in which setting and influence which specific outcomes?

Background

Multiple sclerosis (MS) is a common disease of the nervous system among young adults, with no cure and causing long-term disability. Rehabilitation provides treatments and therapies to lessen the impact of any disability and improve function. Despite recent advances in MS care including rehabilitation, many people with MS are unable to access these developments due to limited mobility, fatigue and related issues, and costs associated with travel. Telerehabilitation is a newer approach to delivering rehabilitation programmes at the patient's home or in the community, using telecommunication technology such as phone lines, video technology, internet applications and others. A wide range of telerehabilitation interventions are trialed in persons with multiple sclerosis, however, evidence for their effectiveness is still unclear.

Study characteristics

This review looked for evidence on how telerehabilitation interventions work in adults with MS. We searched widely for randomised controlled trials (RCTs), a particular kind of study where participants are placed in treatment groups by chance (that is, randomly) because in most settings these provide the highest quality evidence. We were interested in studies that compared a telerehabilitation programme with standard or minimal care, or with different kinds of rehabilitation programmes.

Key results

We found nine relevant RCTs covering 531 participants (469 included in the analyses), evaluating a wide variety of telerehabilitation interventions in persons with MS. The telerehabilitation interventions evaluated were complex, with more than one rehabilitation component and included physical activity, educational, behavioural and symptom management programmes. These interventions had different purposes and used different technologies, so a single overall definite conclusion was not possible. The methodological quality of the included studies is low and varied among the studies.

Quality of evidence

There was 'low-quality' evidence from the included RCTs to support the benefit of telerehabilitation in reducing short-term disability and managing symptoms such as fatigue in adults with MS. We found limited evidence to support the benefit of telerehabilitation interventions in improving disability, reducing symptoms and improving quality of life in the longer term. Furthermore, the interventions and outcomes being investigated in the included studies were different to each other. No studies reported any serious harm from telerehabilitation and there was no information on the associated costs.

There is a need for further research to assess the effects of the range of telerehabilitation techniques and to establish the clinical and cost effectiveness of these interventions in people with MS. The evidence in this review is up to date to July 2014.

Telerehabilitation for persons with multiple sclerosis (Review)

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SUMMARY OF FINDINGS

Summary of findings for the main comparison.

Telerehabilitation for persons with multiple sclerosis

Patient or population: People with multiple sclerosis

Settings: Participants' home, MS regional centres

Intervention: Telerehabilitation

Comparison: Standard care in rehabilitation centres, participants in wait-list, other type/intensity of rehabilitation intervention

Outcomes	No of Participants (studies)	Effect of telerehabilitation interventions for people with multiple sclerosis	Quality of the evidence (GRADE) #
Change in functional activity			
Change in disability directly post-intervention Measures: GLTEQ, DGI, BBS, ARAT, NHPT, 25FWT, CES, VPR Follow-up: depended on the type of intervention; range from (1 month – 12 weeks)	232 (intervention group = 122) (6 studies)	<p>Two studies (Dlugonski 2012; Motl 2011, N = 99) with same cohort of participants showed significant improvement in physical activity in the treatment group at post-intervention assessment as measured by GLTEQ (P < 0.01). Weekly step count (pedometer) increased significantly in the treatment group at post-intervention assessment (P < 0.001)</p> <p>One study (Frevel 2014, N = 18) showed significant improvement in dynamic and static balance capacity compared to baseline values in both intervention group (e-training) (DGI: P = 0.016, BBS: P = 0.011) and control (hippotherapy) group (DGI: P = 0.011, BBS: P = 0.011). There was no difference between groups</p> <p>One study (Huijgen 2008, N = 35) showed no statistically significant differences between intervention and control groups in arm function as measured by ARAT (mean change 1.26, 90% CI -1.90 to 4.42) and NHPT (mean change 7.24, 90% CI -6.55 to 23.25)</p> <p>One study (Paul 2014, N = 30) showed that gait speed measured using 25FWT increased in the intervention group compared to the control group but this was not statistically significant (P = 0.170); and the intervention group showed a statistically significant improvement in the physical subscale of the MSIS (P = 0.048)</p> <p>One study (Gutiérrez 2013a, N = 50) showed improvements in balance and postural control, with a significant increase in CES of the intervention group (mean change; 8.21 points, P < 0.001), but no significant improvement in the control group (mean change: 1.93, P = 0.123). Visual Preference Ratio (VPR) and the contribution of vestibular information (Vestibular Ratio) improved significantly in the intervention group (P < 0.001), but not in the control group (P > 0.05). There were significant post-treatment differences between treatment and control groups in the CES (F = 37.873, P < 0.001) and the VPR (F = 12.156, P < 0.001). Significant post-treatment differences between groups were also found for the ability to accept incorrect visual information expressed by the visual conflict parameter (F = 15.05, P < 0.000). There were no significant between-group differences</p>	⊕⊕⊕⊕ low 1

Telerehabilitation for persons with multiple sclerosis (Review)

		in the contribution of the visual system ($F = 2.64$, $P = 0.11$) or use of somatosensory information ($F = 0.117$, $P = 0.734$) in the maintenance of balance and stability	
Change in short-term disability 3 months or less after the start of the intervention Measures: GLTEQ Follow-up: up to 3 months	45 (intervention group = 22) (1 study)	One study (Dlugonski 2012 , $N = 45$) reported that the treatment group showed a significant increase in physical activity at 3-month follow-up compared to the control group as measured by GLTEQ ($P < 0.001$). There was a non-significant change in assessment scores from post-intervention to 3-month follow-up ($P = 0.61$)	⊕⊕⊕⊕ low ²
Change in long-term disability more than 3 months after the intervention Measure: 6MWT Follow-up: 6 months – 2 years	82 (intervention group = 41) (1 study with 2 reports)	One study with 2 reports (Pilutti 2014 , $N = 82$) showed a significant and positive effect of the intervention on increase in 6MWT distance relative to those in the control group ($P = 0.07$). Physical activity increased most in those with mild disability in the intervention group.	⊕⊕⊕⊕ low ²
Change in symptoms or impairments			
Change in impairments directly post-intervention Measures: FIS, FSS, MFIS, MS Symptom Checklist Follow-up: depended on the type of intervention; range from (1 month – 12 weeks)	265 (intervention group = 138) (4 studies)	<p>One study (Finlayson 2011, $N = 190$) showed a significant reduction in fatigue in intervention group compared to a wait-list control group immediately after intervention as measured by FIS sub-scales (Mean (SD): Cognitive -3.12 (6.1), $P = 0.001$; Physical -2.53 (6.4), $P = 0.014$; Social -6.01 (12.1), $P = 0.002$)</p> <p>One study (Egner 2003, $N = 27$) reported similar fatigue scores (measured using FSS) for all 3 groups (video, telephone and standard care) at 9 weeks post-intervention; however the video group had significantly lower scores than the other 2 groups at month 6 ($P < 0.05$; telephone: $SE = 0.478$; standard care: $SE = 0.536$) and month 18 ($P < 0.05$; telephone: $SE = 0.569$; standard care: $SE = 0.624$)</p> <p>One study (Frevel 2014, $N = 18$) reported that fatigue improved significantly in the control (hippotherapy) group ($P < 0.05$ for all MFIS subscales); while the e-training group improved only on the MFIS cognitive subscale ($P = 0.031$). A significant difference between the groups was noted only in the cognitive subscale of the MFIS ($P = 0.012$)</p> <p>One study (Paul 2014, $N = 30$) reported no improvements in symptoms as measured by MS Symptom Checklist.</p>	⊕⊕⊕⊕ low ³
Change in short-term impairments 3 months or less after the start of the intervention Measures: FIS Follow-up: up to 3 months	190 (intervention group = 94) (1 study)	One study (Finlayson 2011 , $N = 190$) showed a reduction in fatigue at 3 months with large effect size as measured by FIS sub-scales (ES (95% CI): Cognitive 0.58 (0.48 to 0.68); Physical 0.68 (0.55 to 0.82); Social 0.65 (0.53 to 0.77) and FSS scores: -0.38 (-0.45 to -0.31))	⊕⊕⊕⊕ low ⁴
Change in long-term impairments more than	299 (intervention group = 155) (3 studies)	One study (Egner 2003 , $N = 27$) showed a reduction of fatigue measured by FSS in those using video telerehabilitation compared with those using telephone telerehabilitation or standard care groups at 6 months ($P < 0.05$; telephone: $SE = 0.478$;	⊕⊕⊕⊕ low ⁵

3 months after the intervention

Measures: FIS, FSS

Follow-up: 6 months – 2 years

standard care: SE = 0.536) and 18 months ($P < 0.05$; telephone: SE = 0.569; standard care: SE = 0.624). At 12 months follow-up, there was a significant difference in fatigue scores between the video and standard care groups ($P < 0.05$; SE = 0.471)

One study with 2 reports (Pilutti 2014, N = 82) showed a significant and positive effect of the intervention on fatigue severity (FSS, $P = 0.001$) and its physical impact (FIS, $P = 0.008$) at 6-month post-intervention. The results also indicated a favourable effect of the intervention on symptoms of pain (MPQ, $P = 0.08$) and sleep quality post-trial (PSQI, $P = 0.06$), although the differences between groups did not reach statistical significance

One study (Finlayson 2011, N = 190) showed reduction in fatigue at 6 months with a large effect size as measured by FIS subscales (ES (95% CI): Cognitive 0.55 (0.46 to 0.64); Physical 0.61 (0.50 to 0.72); Social 0.67 (0.58 to 0.76) and FSS score: -0.33 (-0.36 to -0.30))

Change in participation

Change in psychological outcomes

Measures: CES-D, HADS, SDMT

Follow-up: variable (range 1 month – 2 years)

139 (intervention group = 76)

(3 studies)

One study (Egner 2003, N = 27) showed no significant difference in depressive symptoms measured by CES-D at end of the intervention period (9 weeks). Mean depression scores were lower in those receiving telerehabilitation by video compared with telephone and standard care group symptoms decreased at 6, 8 and 24 months follow-up. Being male was a significant predictor for an increased depression score at every measurement point except at 24 months ($P < 0.05$). Mean CES-D scores fluctuated throughout each measurement point for all groups, but seemed to decrease at 24 months in all 3 groups, but not statistically significant. Mean depression scores were lower in those receiving telerehabilitation by video compared to telephone and standard care groups and depressive symptoms also decreased at the 6-, 8- and 24-month follow-ups, but this was not significantly different between groups.

One study (Paul 2014, N = 30) reported a small non-significant improvement in anxiety measured by HADS in the control group compared with the treatment group at post-treatment (8 - 9 weeks) ($P = 0.016$)

One study with two reports (Pilutti 2014, N = 82) showed a statistically significant group interaction in psychological outcomes on SDMT scores ($F = 5.68$, $P = 0.02$), which was moderate in magnitude (partial eta squared (η^2) = 0.08). There was a clinically meaningful improvement in SDMT scores in the subgroup with mild disability in the intervention condition (~ 6 points increase, moderate effect size (d) = 0.41), whereas those with moderate disability in the intervention condition demonstrated minimal change (~ 1 point decrease, $d = 0.12$). There were minimal changes in SDMT scores for those with both mild or moderate disability (~ 1 point increase, $d = 0.10$ for both) in the control group. There was also significant improvement in depression and anxiety in the intervention group (with large effect size ($\eta^2 = 0.10$ for both) compared with the control group measured by the HADS (depression: $F = 7.90$, $P = 0.006$; anxiety: $F = 8.00$, $P = 0.006$)

⊕⊕⊕⊕

low ⁶

Change in quality of life

392 (intervention group = 201)

One study (Egner 2003, N = 27) reported no significant difference in QoL measured using QWB at the end of the interven-

⊕⊕⊕⊕

low ⁷

Measures: QWB, HAQUAMS, MSIS-29, SF-36, LMSQOLS, Follow-up: variable (range 1 month – 2 years)

(6 studies, 1 with 2 reports)

tion period (9 weeks). Mean QWB scores for each measurement point (6, 9, 12, 18 and 24 months) were higher (indicating higher QoL) for those in the video group than for the standard care and telephone groups, but were significantly better in the video group compared to the telephone group at month 12 only ($P < 0.05$; $SE = 0.023$). The telephone group and standard care groups reported similar mean QWB scores over the 2-year follow-up period.

One study (Frevel 2014, $N = 18$) showed significant improvement in QoL measured by HAQUAMS (cognition: $P = 0.026$; function of lower limb: $P = 0.008$; mood: $P = 0.045$) in the control group (hippotherapy), but not in the intervention group (e-training)

One study (Dlugonski 2012, $N = 45$) showed non-significant condition-by-time interactions for QoL measured by MSIS-29. There was no significant correlation between changes in QoL from base line to post-intervention in either the treatment or control groups

One study (Finlayson 2011, $N = 190$) showed that significant improvement in HRQoL in the intervention group on the SF-36 subscales except the physical functioning and bodily pain subscales: change score (95% CI): Vitality 6.99 (4.29 to 9.69); Role Emotion 10.08 (4.13 to 16.04); Mental Health 5.78 (3.89 to 7.67); Social Function 7.95 (4.09 to 11.82); General Health 3.61 (1.37 to 5.85); Role Physical 11.12 (6.22 to 16.02)

One study (Paul 2014, $N = 30$) reported non-significant improvement in HRQoL measured by LMSQOLS in the treatment group compared with control group post-treatment (8 - 9 weeks) (mean difference -0.07 vs 1.0)

One study with 2 reports (Pilutti 2014, $N = 82$) reported that participants in the intervention group perceived a positive change in physical HRQoL measured by MSIS-29 ($P = 0.06$)

Change in other outcomes

Cost effectiveness	531 (intervention group = 277) (9 studies)	Not measured in any of the studies	See 'Impact'
Process evaluation (user satisfaction)	80 (intervention group = 46) (2 studies)	<p>One study (Dlugonski 2012, $N = 45$) showed that participants were most satisfied with (mean \pm SD): the overall programme: 4.8 ± 0.4, staff: 4.9 ± 0.2 and pedometer: 4.7 ± 0.6, but slightly less satisfied with the website itself: 4.1 ± 0.9</p> <p>One study (Huijgen 2008, $N = 35$) reported that overall, both participants and therapists were satisfied with the intervention (over 55% in all 6 items). Both participants and therapists were less satisfied with the aesthetic aspect of the system and had difficulty completing tasks</p>	⊕⊕⊕⊕ very low ⁸
Serious adverse events	531 (intervention group = 277) (9 studies)	No serious adverse events reported	See 'Impact'
Caregivers-related outcomes	531 (intervention group = 277) (9 studies)	Not measured in any of the studies	See 'Impact'

ARAT: Action Research Arm Test; **CES:** Composite Equilibrium Score; **CES-D:** Center for Epidemiologic Studies Depression Scale; **CI:** Confidence interval; **DGI:** Dynamic Gait Index; **EDSS:** Expanded Disability Status Scale; **ES:** Effect size; **FIS:** Fatigue Impact Scale; **FSS:** Fatigue Severity Score; **GLTEQ:** Godin Leisure-Time Exercise Questionnaire; **HADS:** Hospital Anxiety and Depression Scale; **HAQUAMS:** Hamburg QoL Questionnaire in MS; **HRQoL:** Health related quality of life; **IQR:** inter quartile range; **LMSQOLS:** Leeds MS Quality of Life Scale; **MPQ:** McGill Pain Questionnaire; **MS:** Multiple Sclerosis; **MSIS-29:** MS Impact Scale; **NHPT:** Nine Hole Peg Test; **PSQI:** Pittsburgh Sleep Quality Index; **QoL:** quality of life; **QWB:** Quality of Well-Being Scale; **SD:** Standard deviation; **SDMT:** Symbol Digit Modalities Test; **SE:** Standard Error; **SF-36:** 36-Item Short Form Health Survey; **SOT:** Sensory organisation Test; **VPR:** Visual Preference Ratio; **6MWT:** 6 Meters Walk Test; **25FWT:** 25 Feet Walk Test; **95% CI:** 95 percent confidence interval

GRADE Working Group grades of evidence

High quality: Further research is very unlikely to change our confidence in the estimate of effect.

Moderate quality: Further research is likely to have an important impact on our confidence in the estimate of effect and may change the estimate.

Low quality: Further research is very likely to have an important impact on our confidence in the estimate of effect and is likely to change the estimate.

Very low quality: We are very uncertain about the estimate.

¹Methods of randomisation not described or poorly described in 4 studies, only 1 study reported blinding of the assessor, and allocation concealment was described in only 1 study

²Unclear randomisation procedure, allocation concealment not reported, no blinding of the participants or assessors

³Methods of randomisation not described or poorly described in 1 study, none of the studies reported blinding of the participants or assessor, and allocation concealment was not described or unclear in 2 studies

⁴No blinding of the participants or assessors, high risk of attrition bias (> 20% drop-out)

⁵Methods of randomisation and allocation concealment not described or poorly described in 2 studies, all 3 studies did not report blinding of the participants or assessor

⁶Methods of randomisation not described or poorly described in 2 studies, none of the studies reported blinding of the participants or assessor and allocation concealment procedure

⁷Methods of randomisation not described or poorly described in 3 studies, allocation concealment procedure described only in 2 studies, and none of the studies reported blinding of the participants or assessor

⁸Methods of randomisation and allocation concealment procedure not described or poorly described, and blinding of the participants or assessor not reported in both studies

BACKGROUND

Description of the condition

Multiple sclerosis (MS) is a chronic neurological disease, characterised by patchy inflammation, gliosis and demyelination within the central nervous system (CNS), that affects approximately 1.3 million people worldwide (WHO 2008). The median estimated incidence of MS globally is 2.5 per 100,000 (with a range of 1.1 to 4) (WHO 2008), the prevalence is about 30 per 100,000 population (range 5 to 80), with a female preponderance (female to male ratio of 3:1) (Trisolini 2010; WHO 2008).

The patterns of presentation in MS are heterogeneous and include: 'relapsing remitting' (RR) MS (85%), characterised by exacerbations and remissions; 'secondary progressive' (SP) MS with progressive disability acquired between attacks (in 70% to 75% who start with RR, it is estimated more than 50% will develop SPMS within 10 years, and 90% within 25 years); 'primary progressive' (PP) MS (10%), where persons develop progressive disability from the onset; and 'progressive relapsing' (PR) MS (5%), where persons begin worsening gradually and subsequently start to experience discrete attacks (MS Australia 2012; Weinshenker 1989). The prognosis in MS is variable and difficult to predict, and depends on the type, severity and location of demyelinating lesions within the CNS (Hammond 2000; MS Australia 2012). Various factors such as older age at onset, progressive disease course, multiple onset symptoms, pyramidal or cerebellar symptoms and a short interval between onset and first relapse are associated with worse prognosis (Hammond 2000). Persons with MS (pwMS) have a prolonged median survival time from the time of diagnosis of approximately 40 years (Weinshenker 1989). Therefore, issues related to progressive disability (physical and cognitive), psychosocial adjustment and social re-integration progress over time. These have implications for pwMS, their carers, treating clinicians and society as a whole, in terms of healthcare access, provision of services and financial burden (Pfleger 2010; Trisolini 2010).

The pwMS can present with various combinations of deficits such as physical (motor weakness, spasticity, sensory dysfunction, visual loss, ataxia), fatigue, pain (neurogenic, musculoskeletal and mixed patterns), incontinence (urinary urgency, frequency), cognitive (memory, attention), psychosocial, behavioural and environmental problems, which limit a person's activity (function) and participation (Khan 2007). Cognitive and behavioural problems can be subtle and often precede physical disability requiring long-term care (Beer 2012). The care needs in this population are complex due to cumulative effects of the impairments and disabilities, the 'wear and tear' and the impact of aging with a disability. Longer-term multidisciplinary management is recommended, both in hospital and in community settings to maintain functional gains and social re-integration (participation) over time (Khan 2007; Khan 2010a; WHO 2008). Despite recent advances in MS management, many pwMS are unable to access these developments due to limited mobility, fatigue and related issues, plus costs associated with travel. With increasing financial constraints on healthcare systems, alternative methods of service delivery in the community and over a longer term are now a priority. Telerehabilitation for pwMS has potential as a tool to improve health care with reduction in care costs (Zissman 2012). The emerging advances in information and communication technology (ICT) may present as an alternative efficient and cost-effective

method to deliver rehabilitation treatment in a setting convenient to the patient, such as their home.

Description of the intervention

The terminology used in ICT in health care is often used interchangeably and includes: 'telemedicine', 'telehealth', 'telehealthcare', 'e-Health', 'e-medicine', 'telerehabilitation' etc. (Currell 2000; McLean 2010; McLean 2011; Winters 2002). In this review we define the term 'telerehabilitation' as 'the use of information and communication technologies as a medium for the provision of rehabilitation services to sites or patients that are at a distance from the provider' (Rogante 2010; Theodoros 2008). The applications to date encompass systems ranging from low-bandwidth, low-cost videophones to highly expensive, fully immersive virtual reality systems with haptic interfaces (Theodoros 2008).

Telerehabilitation extends rehabilitative care beyond the hospital process and facilitates multifaceted, often psychotherapeutic approaches to modern management of pwMS at home or in the community (Huijgen 2008). It provides equal access to individuals who are geographically remote and to those who are physically and economically disadvantaged (Hailey 2011; Rogante 2010) and can improve the quality of rehabilitation delivered (Hailey 2011; Kairy 2009; McCue 2010; Rogante 2010; Steel 2011). It can give healthcare providers an opportunity to evaluate the intervention previously prescribed, monitor adverse events and identify areas in need of improvement. The treating therapists can monitor patients' progress and optimise the timing, intensity and duration of therapy as required, which may not always be possible within the constraints of face-to-face treatment protocols in the current health systems (Hailey 2011; Steel 2011).

How the intervention might work

Telerehabilitation is an emerging method of delivering rehabilitation that uses technology to serve patients, clinicians and systems by minimising the barriers of distance, time and cost. The driving force behind this has been the need for an alternative to face-to-face intervention, enabling service delivery in the natural environment – that is, in patients' homes (Hailey 2011). This method of in vivo delivery of healthcare services can address associated issues of efficacy, problems of generalisation and increasing patient participation and satisfaction with treatment.

The benefits and advantages of telerehabilitation have been well documented (Bendixen 2009; Brennan 2009; Chumbler 2012; Constantinescu 2010; Johansson 2011; Kairy 2009; Lai 2004; Legg 2004; Russell 2011; Steel 2011). A home-based physical telerehabilitation programme was considered feasible and effective in improving function in pwMS (Finkelstein 2008). Telemedicine in pwMS as a tool has the potential for improved health care with reduction in care costs (Zissman 2012). A systematic review that analysed rehabilitation therapies delivered at home in stroke survivors showed positive outcomes, with a reduction in the risk of deterioration, improved ability to perform activities of daily living, reduced costs and duration of rehabilitation in a frail elderly population (Legg 2004). Other reports used telerehabilitation to direct multidisciplinary co-ordinated, goal-directed treatment to monitor clinical progress for patients at a distance (Hailey 2011; Kairy 2009; McCue 2010; Rogante 2010; Steel 2011). In these cases, telerehabilitation

offered an opportunity to provide an individualised rehabilitation intervention beyond the hospital setting, by regular monitoring and evaluation of the patients' needs and progress, with a range of services suited to the individual and their environment (Hailey 2011; Kairy 2009; McCue 2010; Rogante 2010; Steel 2011). Telerehabilitation also provides health outcomes comparable to traditional in-person patient encounters, including improved patient satisfaction (Egner 2003; Finkelstein 2008; Hailey 2011; Huijgen 2008; Kairy 2009). It can encompass single or multiple interventions, or both, aimed at improving the patient experience at the level of impairment, activity or participation, and can educate patients (and carers) in their ongoing self management.

Why it is important to do this review

There is strong evidence to support the effectiveness of rehabilitation programmes for pwMS (Khan 2007; Khan 2010a). With increasing financial constraints on healthcare systems, alternative methods of service delivery in the community and over a longer term are now a priority. Telerehabilitation was reported to be effective in various neurological conditions including MS (Egner 2003; Finkelstein 2008; Huijgen 2008). However, there is as yet no systematic review of telerehabilitation interventions in pwMS to guide treating clinicians on evidence for its validity, reliability, effectiveness and efficiency in this population.

This review analyses published and unpublished clinical trials relating to MS and telerehabilitation, identifies the evidence base for its use, and discusses issues for future expansion of the evidence base by traditional research and other methods.

OBJECTIVES

To investigate the effectiveness and safety of telerehabilitation intervention in persons with multiple sclerosis (pwMS) for improved patient outcomes.

Specifically, the review addresses the following questions:

- Does telerehabilitation achieve better outcomes compared with traditional face-to-face intervention?
- What types of telerehabilitation interventions are effective, in which setting and influence which specific outcomes (impairment, activity limitation and participation)?

METHODS

Criteria for considering studies for this review

Types of studies

We included all randomised controlled trials (RCTs) and controlled clinical trials (CCTs), including quasi-randomised and quasi-experimental designs with comparative controls (where the method of allocation is known but is not considered strictly random).

Types of participants

We included studies in pwMS (18 years and over) with a confirmed diagnosis of MS (McDonald 2001; Polman 2005; Poser 1983) and all disease subgroups (relapsing remitting, secondary progressive and progressive MS).

Types of interventions

We considered all modalities (type, duration, frequency and intensity) of telerehabilitation intervention, using telecommunication technology as the delivery medium, such as internet, videoconferencing, telephone and virtual reality, aimed at achieving patient-centred goals or enhancing function and participation. These included: (a) individual (unidisciplinary) treatments, e.g. physical interventions: exercise, self-management education, etc., and (b) multidisciplinary rehabilitation, i.e. delivered by two or more disciplines: occupational therapy, physiotherapy, exercise physiology, orthotics, other allied health and nursing, in conjunction with medical input.

The settings of telerehabilitation intervention included the following:

- outpatient or day treatment settings in community rehabilitation centres;
- home-based settings, in the patients' own homes and local community.

Control conditions included the following:

- no treatment;
- placebo/sham;
- any type of traditional face-to face rehabilitation treatment in outpatient or day treatment settings.

We excluded studies if they investigated:

- acute medical/surgical/pharmacological interventions for pwMS provided via telemedicine technology in isolation, unless it was administered as a concomitant intervention along with the telerehabilitation intervention, which was administered in the same way in both control and treatment groups;
- studies on telerehabilitation targeting mental health conditions or substance abuse;
- studies on home care (or tele-home care) with no rehabilitation objectives;
- studies on satisfaction with or acceptance of telerehabilitation technology;
- studies on technical development or feasibility of telerehabilitation;
- studies exploring telerehabilitation technology for intra-professional communication (such as for second opinions) and for passive information provision, e.g. online education, where there is no direct interaction or involvement of a healthcare professional with the patient.

Types of outcome measures

We identified diverse outcomes, given the varied presentations of MS-related problems and goals of treatment related to MS severity. The specific outcome measures per se were not part of the exclusion criteria for this review. We report and list all outcome measures used in studies in Table 1.

Primary outcomes

We categorised primary outcomes according to the International Classification of Functioning, Disability and Health (ICF; WHO 2001), and included:

- improvement in *functional* activity; such as activities of daily living (ADL), mobility, continence, etc.;
- improvement in symptoms or *impairments*, e.g. pain, spasm frequency, joint range of movement, involuntary movements, spasticity, etc.;
- improvement in *participation* and *environmental* or *personal context*, or both; e.g. quality of life (QoL), psychosocial function, employment, education, social and vocational activities, patient and carer mood, relationships, social integration, etc.

We included the measure of achievement of intended goals for treatment, e.g. goal attainment scaling or other measure of goal achievement.

It should be noted, however, that some outcome scales crossed boundaries between these ICF concepts, for example, items relating both to impairment (symptoms) and activity.

Secondary outcomes

These reflect compliance with the intervention, service utilisation, and cost effectiveness of telerehabilitation compared with traditional rehabilitation interventions.

We report all adverse events that may have resulted from the intervention. A serious adverse event is defined 'as an event that is life-threatening or requires prolonged hospitalisation' (Khan 2007). We also explored carer-related issues, such as carer strain.

Timing of outcome measures

The time points for outcome assessments were: short-term (immediately after intervention or up to three months) and long-term (greater than three months) from the start of the intervention. We considered patient follow-up assessments similarly as short-term (up to three months) and long-term follow-up (greater than three months) after cessation of the intervention.

Search methods for identification of studies

We considered articles in all languages with a view to translation, if necessary. We extracted trials coded with the specific key words and considered them for inclusion in the review.

Electronic searches

The review authors, along with the Trials Search Co-ordinator, searched the Cochrane Multiple Sclerosis and Rare Diseases of the Central Nervous System Group Specialised Register, last searched on 9 July 2014, which contains the following:

1. The Cochrane Central Register of Controlled Trials (CENTRAL) (2014 Issue 7).
2. MEDLINE (PubMed) (1966 to 9 July 2014).
3. EMBASE (EMBASE.com) (1974 to 9 July 2014).
4. Cumulative Index to Nursing and Allied Health Literature (CINAHL) (EBSCO host) (1981 to 9 July 2014).
5. Latin American and Caribbean Health Science Information Database (LILACS) (Bireme) (1982 to 9 July 2014).
6. Clinical trial registries; clinicaltrials.gov.
7. World Health Organization (WHO) International Clinical Trials Registry Portal (apps.who.int/trialsearch/).

The keywords used to search for studies for this review are listed in [Appendix 1](#).

Information on the Trial Register of the Review Group and details of search strategies used to identify trials can be found in the 'Specialised Register' section within the Cochrane Multiple Sclerosis and Rare Diseases of the Central Nervous System Group [module](#).

Searching other resources

We performed an expanded search to identify articles potentially missed through the database searches and articles from 'grey literature' from 1996 to latest date. This included the following:

- handsearches of reference lists of all retrieved articles, texts and other reviews on the topic;
- handsearches of the most relevant journals related to MS and spasticity research and treatment (such as, but not limited to: *Archives of Physical Medicine and Rehabilitation*, *Journal of Rehabilitation Medicine*, *Journal of Neurology*, *Journal of Neurology, Neurosurgery and Psychiatry*, *Clinical Rehabilitation*, *Neurology*, *Physical Therapy*, *Multiple Sclerosis*, *Telemedicine Journal and e-Health*, *Journal of Medical Internet Research* and others);
- searches using the 'Related articles' feature (via PubMed);
- searches of ProQuest Dissertations and Theses;
- searches of Web of Science for citation of key authors;
- searches of System for Information on Grey Literature in Europe (SIGLE);
- contacting local and foreign experts for further information, such as MS Groups/Associations, the Cochrane MS Group, key authors of publications in this review;
- contacting authors and researchers active in this field.

We also searched the following websites for ongoing and unpublished trials:

- Current Controlled Trials (www.controlled-trials.com);
- UK Clinical Research Network Portfolio Database (public.ukcrn.org.uk/search/).

Data collection and analysis

Selection of studies

Two review authors (BA, FK) independently screened and short-listed all abstracts and titles of studies identified by the search strategy for appropriateness based on the selection criteria. We independently evaluated each study from the shortlist of potentially appropriate studies for inclusion or exclusion. We obtained the full text of the article for further assessment to determine if the trial met the inclusion criteria. If we could not reach a consensus about the inclusion or exclusion of any individual study, we made a final consensual decision by discussion amongst all the review authors. We had intended to submit the full article to the editorial board for arbitration when there was no consensus regarding the inclusion or exclusion of a study between the review authors; however, this was not necessary. We were not masked to the name(s) of the study author(s), institution(s) or publication source at any level of the review.

We had planned to seek further information, where necessary, about the method of randomisation or a complete description of the telerehabilitation interventions from the trialists, but this was not required.

Data extraction and management

Two review authors (BA, FK) independently extracted data from each study that met the inclusion criteria, using a standardised data collection form, with other review authors (JK, MG) making a final check. We had intended to contact the primary authors of eligible studies to provide data and clarification where adequate data were not reported, but this was not required. We summarise all studies that met the inclusion criteria in the 'Characteristics of included studies' table provided in Review Manager 5 software developed by Cochrane (Review Manager 2014), and include details on design, participants, interventions and outcomes.

We report the following information from individual studies:

- publication details;
- study design, study setting, inclusion and exclusion criteria, method of allocation, risk of bias;
- participant population, e.g. age, type of MS, disease duration, disability (according to Kurtzke's Expanded Disability Status Scale (EDSS) score (Kurtzke 1982);
- details of intervention;
- outcome measures (primary and secondary);
- withdrawals, compliance, length and method of follow-up and number of participants followed up.

We extracted data for every participant assessed for each outcome measure, and for dichotomous data the number in each treatment group and the numbers experiencing the outcome of interest where possible. We extracted data for intention-to-treat (ITT) analysis from each study, and where ITT data were not available, we retrieved 'on-treatment' data or the data of those who completed the trial. We resolved any disagreement by recourse to other review authors (JK, MG) and through discussion, with reference to the original report. We had planned to contact study authors for additional information and data if necessary, but this was not required. We present the results in a tabulated format in the [Summary of findings for the main comparison](#).

Assessment of risk of bias in included studies

Three review authors (BA, FK, MG) independently assessed the methodological quality of the included studies using the Cochrane 'Risk of bias' tool (Higgins 2011) for sequence generation, allocation concealment, blinding of participants, therapists and outcome assessors, incomplete outcome data and selective outcome reporting. Further, we also checked baseline data amongst the study groups for stability.

We considered a study to be of 'high' methodological quality if the risks of bias for all domains were low. We termed this a 'high-quality study'. We rated a study as being of 'low' methodological quality where there was a lack of clarity or a high risk of bias for one or more domains, and termed this as a 'low-quality study'. If we rated most domains at high risk of bias, we rated the study as a 'very low-quality study'. We resolved any disagreements by consensus between the review authors. We present results using 'Risk of bias' summary figures.

Measures of treatment effect

A quantitative analysis was not possible due to clinical heterogeneity (see below), the use of diverse methodology, interventions and outcome measures, and insufficient data available. We entered and analysed all data in Review Manager 5 software (Review Manager 2014). We qualitatively summarised the studies in the [Characteristics of included studies](#) tables, presented the results of primary and secondary outcomes of included studies, categorised according to the ICF framework, in the [Summary of findings for the main comparison](#). We describe the results in a narrative form in the [Discussion](#) section below. If studies had been available, and if meta-analyses become feasible in future updates, we will analyse treatment effects as described in the protocol version of this review (Khan 2013).

Unit of analysis issues

For each study, we assessed the appropriate units of analysis, which included the level at which randomisation occurred (e.g. parallel-group design, cluster-randomised trials, cross-over trials, etc.), type, duration, intensity and setting of telerehabilitation interventions.

Dealing with missing data

We provide information about missing data related to participants dropping out or lost to follow-up in the [Characteristics of included studies](#) tables. We contacted the primary authors to obtain additional information and clarification by personal communication (email), to clarify possible overlapping of the data in the four eligible studies. We did not perform imputation of missing data as we were not able to perform meta-analyses.

Assessment of heterogeneity

We assessed clinical heterogeneity by examining the characteristics of studies, the similarity between the types of participants, settings, interventions (frequency, intensity, duration) and outcomes, as specified in the [Criteria for considering studies for this review](#) section. Due to apparent clinical heterogeneity, a comprehensive quantitative analysis (meta-analysis) was not possible. We did not assess statistical heterogeneity and presented the studies separately. We will consider both clinical and statistical heterogeneity, if data become available in future updates, as described in the protocol version of this review (Khan 2013).

Assessment of reporting biases

We used a comprehensive search strategy, which included searching for unpublished studies (grey literature), and searching trials registers (See [Search methods for identification of studies](#)) to avoid reporting biases and publication bias (Egger 1998). We did not analyse trial data using funnel plots to investigate the likelihood of publication bias, due to the small number of included studies.

Data synthesis

There was a wide variation in several variables of the included studies, such as MS course and severity, content; frequency, duration, mode of delivery and aim of the interventions; outcome measures used; presentation of results; and methodological quality. Because of the observed heterogeneity, we did not pool data for a quantitative analysis. If studies had been available and if data become available in future updates, we will attempt a quantitative analysis, as described in the protocol version of this

review ([Khan 2013](#)). We have highlighted the strength of study findings, discussed gaps in the current literature and identified future research directions in the [Discussion](#) section.

Subgroup analysis and investigation of heterogeneity

We were unable to perform subgroup analysis for the following subgroups, owing to the lack of available data:

1. Type of telerehabilitation intervention (unidisciplinary or multidisciplinary, or both).
2. Type of MS (relapsing remitting, progressive)
3. Severity of MS (i.e. EDSS < 6; > 6)
4. Duration of follow-up of participants (≤ 3 months; > 3 months)

Sensitivity analysis

We were not able to conduct sensitivity analyses due to our narrative presentation of the results of the included studies. If studies had been available, and heterogeneity existed across trials, we would have conducted sensitivity analyses by omitting trials with a high risk of bias as described in the *Cochrane Handbook for Systematic Reviews of Interventions* ([Higgins 2011](#)). If meta-analyses become feasible in future updates, we will perform sensitivity analyses as described in the protocol version of this review ([Khan 2013](#)).

'Summary of findings' table

These outcomes are included in the [Summary of findings for the main comparison](#):

1. Change in disability (post-intervention, ≤ 3 months, > 3 months)
2. Change in impairments (post-intervention, ≤ 3 months, > 3 months)
3. Change in participation (psychological outcomes, QoL)

4. Cost effectiveness
5. Process evaluation
6. Serious adverse events
7. Caregivers'-related outcomes

We used the five GRADE considerations (risk of bias, inconsistency, imprecision, indirectness and publication bias) to assess the quality of a body of evidence as it relates to the studies that contribute data to the meta-analyses for prespecified outcomes. We used the methods and recommendations described in Section 8.5 and Chapter 12 of the *Cochrane Handbook for Systematic Reviews of Interventions* ([Higgins 2011](#)) using GRADEpro software ([GRADEpro 2008](#)). We justified all decisions to downgrade or upgrade the quality of studies by using footnotes, and we made comments to aid readers' understanding of the review when necessary.

RESULTS

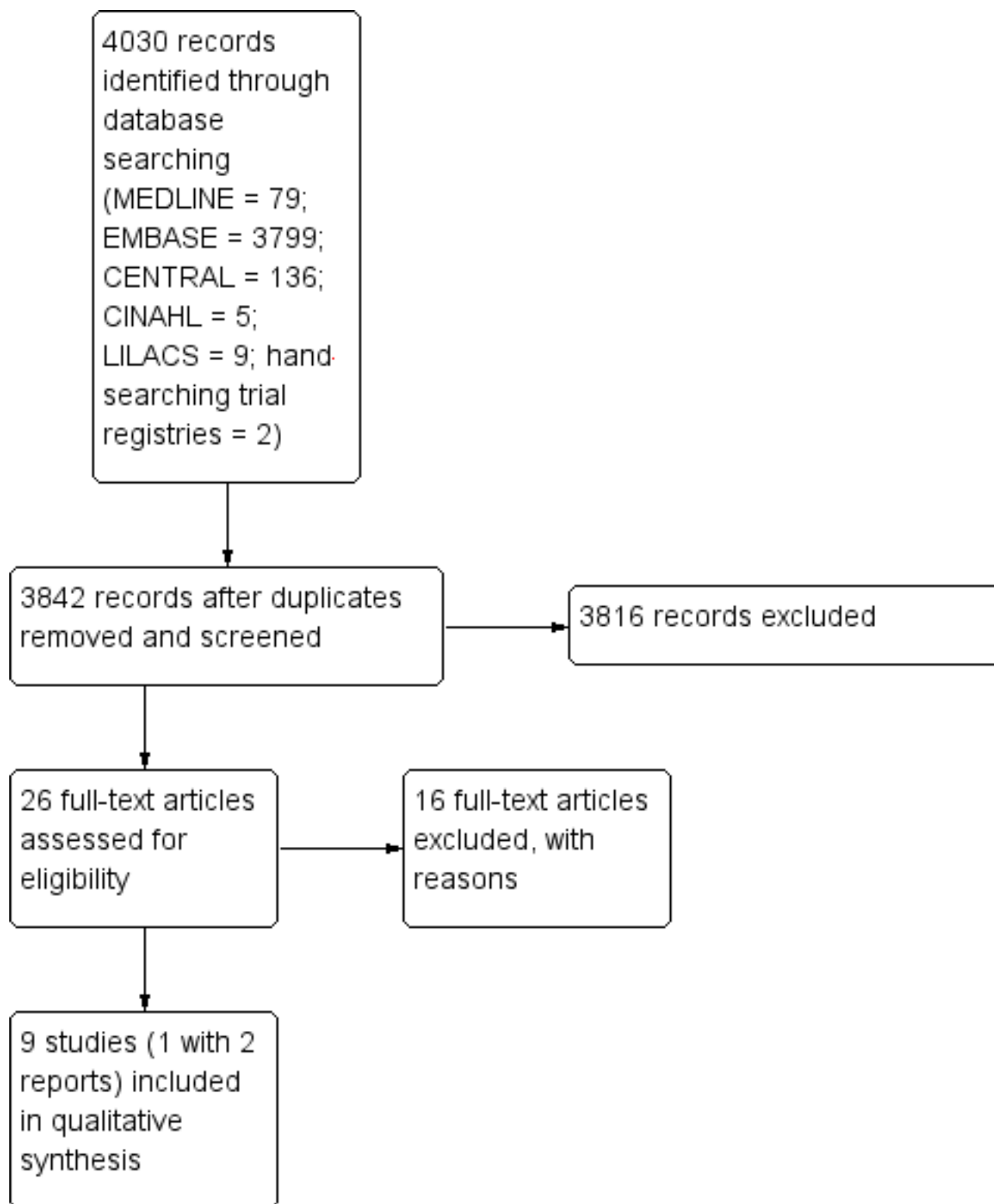
Description of studies

See: [Characteristics of included studies](#); [Characteristics of excluded studies](#)

Results of the search

Electronic and manual searches identified 4030 references (MEDLINE = 79; EMBASE = 3799; CENTRAL = 136; CINAHL = 5; LILACS = 9; CRD database = 0; Cochrane Opportunity Fund Project = 0; Trial Registries via WHO Portal = 0; handsearching journals = 0; handsearching trial registries = 2) with our search criteria. After elimination of duplicates records, we screened the remaining 3842 for closer scrutiny. Of these, we retrieved the full text of 29 articles for further assessment to determine inclusion in the review. We did not identify any ongoing or unpublished studies awaiting classification. See: [Figure 1](#) for Study flow chart.

Figure 1. Study flow diagram.



Included studies

In total, nine RCTs, one with two reports (Pilutti 2014; Sandroff 2014), published between 2003 and 2014 (Dlugonski 2012; Egner 2003; Finlayson 2011; Frevel 2014; Gutierrez 2013a; Huijgen 2008;

Motl 2011; Paul 2014; Pilutti 2014) fulfilled the inclusion criteria for this review (see [Characteristics of included studies](#) table).

Five of the included studies were conducted in the United States (Dlugonski 2012; Egner 2003; Finlayson 2011; Motl 2011; Pilutti

2014); one each was conducted in Spain (Gutiérrez 2013a), Germany (Frevel 2014) and the United Kingdom (Paul 2014), while one was a multicentre study conducted in three different countries (Italy, Spain and Belgium; Huijgen 2008). Three studies were conducted by the same group of authors in the same setting and with the same cohort of participants recruited from a single database (Dlugonski 2012; Motl 2011; Pilutti 2014), of which one reported different outcomes in two different articles (Pilutti 2014).

Participants

Participants' detailed information, including inclusion/exclusion criteria and baseline demographics, are listed in the [Characteristics of included studies](#) table. The nine included studies involved a total of 531 participants (277 participants in the treatment groups and 254 in the control groups). The number of participants in the studies ranged from 27 to 190 (median 45). As expected, there were more women, with their proportion ranging from 56% to 87% (mean 74%). The mean age of participants varied from 41 to 52 years (mean 46.5 years) and mean years since diagnosis from 7.7 to 19.0 years (mean 12.3 years). The majority of participants had a relapsing-remitting course of MS (RRMS), two studies involved only people with RRMS (Dlugonski 2012; Motl 2011) and two studies did not provide details of MS type (Egner 2003; Huijgen 2008). The study inclusion criteria varied between trials. All trials included participants with definite MS, although only two trials specified the commonly-used McDonald's criteria (McDonald 2001) (Frevel 2014; Gutiérrez 2013a). One study reported secondary data regarding MS participants which were collected as part of a larger study of a telerehabilitation intervention in people with severe mobility impairment (Egner 2003).

Intervention

Detailed information about interventions in the included studies is presented in the [Characteristics of included studies](#) tables and is further summarised in [Table 2](#). The various telerehabilitation interventions in the included studies consisted generally of physical activity and educational components.

- Three studies used similar internet-delivered, social cognitive theory-based behavioural intervention to increase physical activity (Dlugonski 2012; Motl 2011; Pilutti 2014)
- One study evaluated a structured in-home education and counselling session delivered via telephone or video by a rehabilitation nurse (Egner 2003)
- One study examined a group-based, teleconference-delivered fatigue management programme (Finlayson 2011)
- One study evaluated a telerehabilitation intervention for arm/hand function at home - the 'Home Care Activity Desk' (HCAD), which consists of a set of exercises for functional activity of the upper limb (Huijgen 2008)
- One study evaluated the effectiveness of an individualised web-based physiotherapy programme (Paul 2014)
- One study published in two different journals by the same authors (Gutiérrez 2013a; Gutiérrez 2013b) examined

the effectiveness of an individualised virtual reality telerehabilitation programme for improvement in postural control

- One study examined the effectiveness of an internet-based home training programme (e-Training) in comparison with hippotherapy to improve balance (Frevel 2014)

The duration and intensity of the telerehabilitation interventions varied significantly depending on the nature of the intervention, and ranged from one to six months (median 12 weeks). None of the studies reported the recruitment time period. The follow-up periods varied between trials, but all studies assessed the participants immediately after intervention. Only one trial reported long-term follow-up of up to 24 months (Egner 2003). For details of assessment time points for each trial refer to the [Characteristics of included studies](#) tables.

Excluded studies

We excluded 16 studies after appraisals of the full reports (listed in the [Characteristics of excluded studies](#) tables). The primary reason for exclusion was:

- 10 studies addressed mental health care as a primary intervention (Amato 2014; Beckner 2010; Cerasa 2013; Fischer 2013; Mohr 2000; Mohr 2005; Mohr 2007; Moss-Morris 2012; Solari 2004; Stuifbergen 2012)
- One study had a medical-care intervention only (Zissman 2012)
- One study evaluated the effectiveness of an online fatigue self-management programme for people with various chronic neurological conditions including MS, but did not provide a subgroup analysis for the MS cohort (Ghahari 2010)
- Two studies assessed counselling interventions for health promotion and major depression (Bombardier 2008; Bombardier 2013)
- Two studies assessed interventions with no rehabilitation objectives, such as education, self management (Miller 2011; Wiles 2003)

Risk of bias in included studies

See: 'Risk of bias' tables in the [Characteristics of included studies](#) and [Figure 2](#) and [Figure 3](#).

[Figure 2](#) and [Figure 3](#) represent the review authors' judgements about each methodological quality item, presented as percentages across all included studies and a summary of the risk of bias, respectively. Where studies failed to report sufficient methodological detail to assess the potential risk of bias, we graded them as being at 'unclear' risk (presented as symbol '?' in [Figure 3](#)). The methodological quality of the nine included trials was 'low', with substantial flaws in the methodological design and a high risk of bias related to their randomisation procedure; blinding of participants, therapists and outcome assessors, and outcome analysis.

Figure 2. Risk of bias graph: review authors' judgements about each risk of bias item presented as percentages across all included studies.

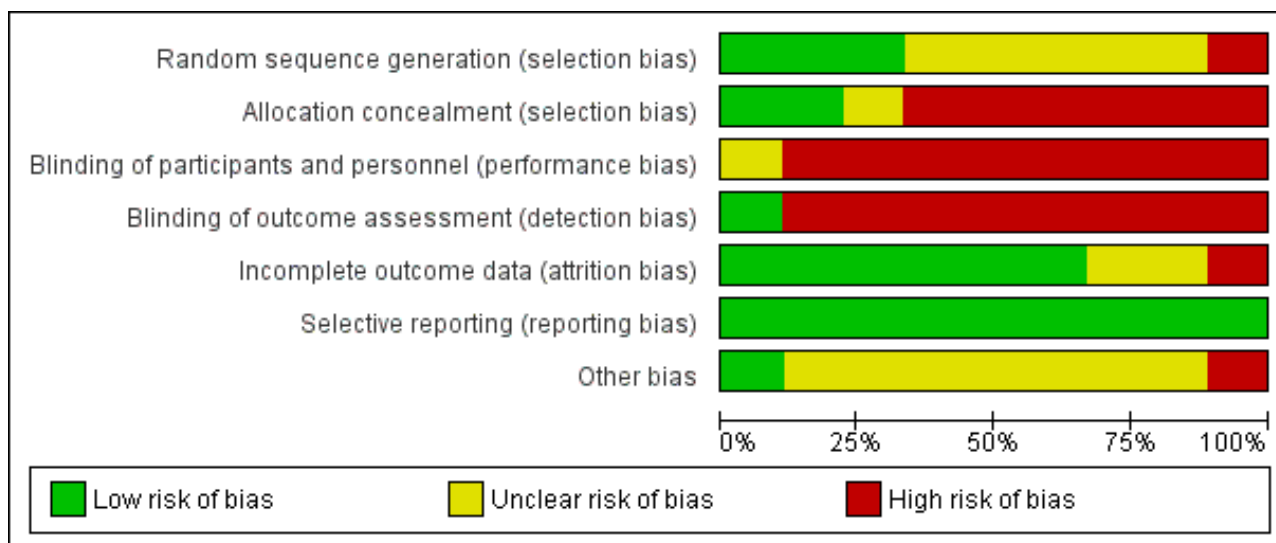


Figure 3. Risk of bias summary: review authors' judgements about each risk of bias item for each included study.

	Random sequence generation (selection bias)	Allocation concealment (selection bias)	Blinding of participants and personnel (performance bias)	Blinding of outcome assessment (detection bias)	Incomplete outcome data (attrition bias)	Selective reporting (reporting bias)	Other bias
Dlugonski 2012	?	-	-	-	+	+	?
Egner 2003	?	?	-	-	+	+	?
Finlayson 2011	+	+	?	-	-	+	?
Frevel 2014	+	+	-	-	+	+	?
Gutiérrez 2013a	-	-	-	+	+	+	-
Huijgen 2008	?	-	-	-	?	+	?
Motl 2011	?	-	-	-	?	+	+
Paul 2014	+	-	-	-	+	+	?
Pilutti 2014	?	-	-	-	+	+	?

Allocation

Although all included studies stated that the procedure was randomised, the methods of randomisation were adequately reported in only six studies (one with two reports) (Dlugonski 2012; Finlayson 2011; Frevel 2014; Motl 2011; Paul 2014; Pilutti 2014).

- Two studies used a random number generator for randomisation (Dlugonski 2012; Pilutti 2014)
- One study used a random permuted block design (Finlayson 2011)
- One randomly allocated the participants using simple allocation by drawing lots of preshuffled opaque envelopes (Frevel 2014)
- One study used a series of random numbers generated in Microsoft Excel (consecutive numbers allocated, where even numbers represented the intervention group and odd numbers the control group) (Paul 2014)

Only three studies described in detail concealment of allocation prior to entry to the study (Finlayson 2011; Frevel 2014; Motl 2011). Other studies either gave little or no information about the randomisation procedure, or used non-random components like alternation, assignment to comparable groups with respect to clinical and demographic factors, or allocation of participants to the intervention group after initial randomisation.

Blinding

Blinding of participants and treating personnel can be challenging in rehabilitation trials, because of the characteristics of interventions. However, blinding of outcome assessors is possible and highly desirable (Amatya 2013). The blinding of participants and personnel was insufficiently reported in most of the studies. Only one study took measures to blind participants to group allocation (Finlayson 2011). None of the studies attempted to blind the treating personnel. One study mentioned blinding of the outcome assessors, but provided no details (Gutiérrez 2013a).

Incomplete outcome data

The drop-out rate of participants during the trial period ranged from 0% to 21%. In four studies, there were no or minimal losses to follow-up (Dlugonski 2012; Egner 2003; Gutiérrez 2013a; Paul 2014). Drop-outs and withdrawals were higher than 20% in only one study (Finlayson 2011), which recruited the highest number of participants. One study which included MS participants as one of the subgroups failed to report the attrition rate (Huijgen 2008). Most of the studies did not conduct intention-to-treat analysis.

Selective reporting

All the included studies reported prespecified (primary and secondary) outcomes (see Table 1 and Table 3 for a list of the outcome measures).

Other potential sources of bias

Sample sizes were small (< 40 participants) in four studies (Egner 2003; Frevel 2014; Huijgen 2008; Paul 2014). A series of three studies was conducted by the same group of authors, which recruited selective participants who volunteered for research through a single database for the same institutions (Dlugonski 2012; Motl 2011; Pilutti 2014). Although none of these studies mentioned overlapping of the recruited participants, we cannot rule out the possibility of inclusion of the same participants in different trials.

Furthermore, this series of studies published one trial (Pilutti 2014) with different outcomes in another report (Sandroff 2014). Most included studies had short-term follow-up, and were restricted to immediate post-treatment assessments. Most studies seemed to be underpowered and only one study performed a sample size calculation (Finlayson 2011). One study (Egner 2003) failed to report the participant recruitment process and methodology in detail, and allocation of participants to treatment and control groups was unbalanced in two studies (Egner 2003; Huijgen 2008).

Effects of interventions

See: [Summary of findings for the main comparison](#)

Meta-analysis was not possible due to the heterogeneity of the included studies mentioned earlier. The included studies used a range of telerehabilitation approaches in pwMS (see Table 2 for the summary of telerehabilitation interventions) and a broad range of outcome measures (see Table 3 for a list of outcome measure used). A summary of the findings of the included trials is presented based on primary and secondary outcomes categorised according to the International Classification of Functioning, Disability and Health (ICF) framework in the [Summary of findings for the main comparison](#). Pooling of data from the included studies was confounded by the differences between interventions and the use of different outcome measures, as highlighted above.

Primary outcomes

Improvement in functional activity

All studies except two (Egner 2003; Finlayson 2011) assessed the first prespecified primary endpoint to improve functional activity in pwMS (N = 314 participants, *low quality evidence*). All studies evaluated participants immediately after the intervention, using different instruments (see Table 3 and [Summary of findings for the main comparison](#)), with intervention periods ranging from one to six months. Overall six studies assessed the functional endpoint post-intervention up to 12 weeks (Dlugonski 2012; Frevel 2014; Gutiérrez 2013a; Huijgen 2008; Motl 2011; Paul 2014).

Two studies (Dlugonski 2012; Motl 2011) conducted in different time periods with the same cohort of participants showed significant improvement in physical activity in the treatment group at the post-intervention assessment, as measured by the Godin Leisure-Time Exercise Questionnaire (GLTEQ) (P < 0.01). The authors' reported increase in physical activity was sustained at three-month follow-up compared with the control group (P < 0.001) (Motl 2011).

One study (Frevel 2014) comparing two interventions, e-training and hippotherapy, showed significant improvement in dynamic and static balance capacity compared with baseline values in both the intervention (e-training) (Dynamic Gait Index (DGI): P = 0.016, Berg Balance Scale (BBS): P = 0.011) and control (hippotherapy) groups (DGI: P = 0.011, BBS: P = 0.011). However, there was no difference between groups.

Huijgen 2008 showed no statistically significant differences between the intervention using telerehabilitation for arm functions (Home Care Activity Desk (HCAD)) and control groups in arm function as measured by Action Research Arm Test (ARAT) (mean change 1.26, 90% confidence interval (CI) -1.90 to 4.42) and Nine-Hole Peg Test (NHPT) (mean change 7.24, 90% CI -6.55 to 23.25).

Paul 2014 reported an increase in gait speed using the 25 Foot Walk Test (25FWT) in the intervention group compared with the control group, but this was not statistically significant ($P = 0.170$). The intervention group had a statistically significant improvement in the physical subscale of the Multiple Sclerosis Impact Scale (MSIS) ($P = 0.048$).

Another study (Gutiérrez 2013a) showed improvements in balance and postural control, with a significant increase in Composite Equilibrium Score (CES) in the intervention group (mean change 8.21 points, $P < 0.001$), but not in the control group (mean change 1.93, $P = 0.123$). Visual Preference Ratio and contribution of vestibular information (VEST, Vestibular Ratio) improved significantly in the intervention group ($P < 0.001$), but not in the control group ($P > 0.05$). There were significant post-treatment differences between treatment and control groups in the CES ($F = 37.873$, $P < 0.001$) and the VEST ($F = 12.156$, $P < 0.001$). Significant post-treatment differences between groups were also found for the ability to accept incorrect visual information expressed by the visual conflict parameter ($F = 15.05$, $P < 0.000$), which demonstrates that the treatment group showed a greater ability to accept post-treatment afferent inputs compared with the control groups. There were no significant between-group differences in the contribution of the visual system ($F = 2.64$, $P = 0.11$) or use of somatosensory information ($F = 0.117$, $P = 0.734$) in the maintenance of balance and stability.

One study (Sandroff 2014) evaluating an internet-delivered behavioural intervention, showed a significant positive effect of the intervention on the Six Minute Walk (6MW) test relative to the control group ($P = 0.07$). The authors also found physical activity increased most in those with mild disability.

Improvement in impairments

Five studies assessed the prespecified primary endpoint (improvement in impairments) using different measures ($N = 347$ participants; *low quality evidence*) (Egner 2003; Finlayson 2011; Frevel 2014; Paul 2014; Pilutti 2014).

Fatigue was the primary outcome in three studies (Egner 2003; Finlayson 2011; Pilutti 2014), all reporting significant differences between groups in favour of the intervention group. One study (Finlayson 2011) showed a significant reduction in fatigue in the intervention group immediately after intervention compared to a wait-list control group as measured by the Fatigue Impact Scale (FIS) in all three subscales: mean difference (SD): Cognitive -3.12 (6.1), $P = 0.001$; Physical -2.53 (6.4), $P = 0.014$; Social -6.01 (12.1), $P = 0.002$. These changes were maintained with large effect sizes in all FIS subscales at three-month follow-up: Effect Size (95% CI): Cognitive 0.58 (0.48 to 0.68); Physical 0.68 (0.55 to 0.82); Social 0.65 (0.53 to 0.77), and at six-month follow-up: Cognition: 0.55 (0.46 to 0.64); Physical: 0.61 (0.5 to 0.72) and Social: (0.67 (0.58 to 0.76). There was also a significant reduction in the Fatigue Severity Scale (FSS) scores at all three time periods.

Egner 2003 analysed the impact of a telerehabilitation intervention (structured in-home counselling and education) delivered via telephone or video, and reported similar fatigue scores (measured using FSS) for all three groups (video, telephone and standard care) at nine weeks post-intervention; however, the participants in the video group had significantly lower scores than the other two groups at six months ($P < 0.05$) and at 18 months ($P < 0.05$).

One study (Pilutti 2014) showed a significant positive effect of the behavioural intervention on fatigue severity (FSS, $P = 0.001$) and its physical impact (FIS, $P = 0.008$) at six-month post-intervention. There was a favourable effect of the intervention on symptoms of pain (McGill Pain Questionnaire (MPQ), $P = 0.08$) and sleep quality post-trial (Pittsburgh Sleep Quality Index (PSQI), $P = 0.06$), although the differences between groups did not reach statistical significance.

Frevel 2014 reported significant improvement in fatigue in the control group (hippotherapy) ($P < 0.05$) for all subscales of the Modified Fatigue Impact Scale (MFIS), while the intervention group (e-training) improved only on the MFIS cognitive subscale ($P = 0.031$). A significant difference between the groups was noted only in the cognitive subscale of the MFIS ($P = 0.012$).

One study (Paul 2014) reported no improvements in symptoms as measured by the MS Symptom Checklist.

Improvement in participation

Psychological outcomes

Overall three studies (one with two reports), assessed cognitive functions as one of the outcomes ($N = 139$ participants, *low quality evidence*) (Egner 2003; Paul 2014; Pilutti 2014).

Egner 2003 showed that a telerehabilitation intervention (structured in-home counselling and education) delivered via telephone or video, improved depressive symptoms as measured by the Centre for Epidemiologic Studies Depression Scale (CES-D) at the end of the intervention period (nine weeks) in both groups. Mean CES-D scores fluctuated, but decreased at 24 months in all three groups. This was, however, not statistically significant. Mean depression scores were lower in those receiving telerehabilitation by video compared with telephone and standard-care groups, and depressive symptoms also decreased at the six-, eight- and 24-months follow-ups, but this was not significantly different between groups. The authors reported that being male was a significant predictor for increased depression score at every measurement point except at 24 months ($P < 0.05$) (Egner 2003).

Paul 2014 reported a small non-significant improvement in anxiety measured by the Hospital Anxiety and Depression Scale (HADS) in the control group compared to the treatment group post-treatment (eight to nine weeks) ($P = 0.016$).

One study with two reports (Pilutti 2014) showed a statistically significant group interaction in psychological outcomes on Symbol Digit Modalities Test (SDMT) scores ($F = 5.68$, $P = 0.02$), which was moderate in magnitude (partial eta squared (η^2) = 0.08). There was a clinically meaningful improvement in SDMT scores in the subgroup with mild disability in the intervention condition (~ 6 points increase, moderate effect size (d) = 0.41), whereas those with moderate disability in the intervention condition demonstrated minimal change (~ 1 point decrease, $d = 0.12$). There were minimal changes in SDMT scores for those with mild or moderate disability (~ 1 point increase, $d = 0.10$ for both) in the control group. There was also significant improvement in depression and anxiety in the intervention group (with large effect size (η^2) = 0.10 for both) compared with the control group measured by the HADS (depression: $F = 7.90$, $P = 0.006$; anxiety: $F = 8.00$, $P = 0.006$) (Pilutti 2014).

Quality of life

Six studies assessed quality of life (QoL), using different outcome measures (N = 392 participants; *low quality evidence*) (Dlugonski 2012; Egner 2003; Finlayson 2011; Frevel 2014; Paul 2014; Pilutti 2014).

Egner 2003 reported no significant difference in QoL between the treatment groups (video or telephone) and control group (standard care) measured using the Quality of Well-Being Scale (QWB) at the end of the intervention period (nine weeks). However, mean QWB scores for each measurement point (6-, 9-, 12-, 18- and 24-months) were higher (indicating higher QoL) for participants in the video group than for those in the standard care and telephone groups. There were significantly higher QWB scores in the video compared with the telephone groups at 12 months follow-up only ($P < 0.05$; standard error (SE) = 0.023). The telephone group and standard-care groups reported similar mean QWB scores over the two-year follow-up period (Egner 2003).

One study (Frevel 2014) showed significant improvement in QoL measured by the Hamburg Quality of Life Questionnaire in Multiple Sclerosis (HAQUAMS) (in subscales - Cognition: $P = 0.026$; Function of lower limb: $P = 0.008$; Mood: $P = 0.045$) in the control group (hippotherapy), but not in the intervention group (e-training).

Finlayson 2011 reported that a fatigue management programme showed significant improvement in QoL in the intervention group on the 36-item Short Form Health Survey Questionnaire (SF-36) in all subscales except physical functioning and bodily pain (change score (95% CI)): Vitality 6.99 (4.29 to 9.69); Role Emotion 10.08 (4.13 to 16.04); Mental Health 5.78 (3.89 to 7.67); Social Function 7.95 (4.09 to 11.82); General Health 3.61 (1.37 to 5.85); Role Physical 11.12 (6.22 to 16.02).

Two studies (Dlugonski 2012; Pilutti 2014) assessed QoL using the Multiple Sclerosis Impact Scale (MSIS-29) and found no significant correlation between changes in QoL from baseline to post-intervention in either treatment or control groups.

Similar non-significant improvement in QoL was reported in another study (Paul 2014), at post-treatment (eight to nine weeks), in which authors used the Leeds Multiple Sclerosis Quality of Life Scale (LMSQOL) (mean difference in treatment group: -0.07 versus control group: 1.0).

Secondary outcomes

Two studies (Dlugonski 2012; Huijgen 2008) reported process evaluation (satisfaction and acceptance of the telerehabilitation).

Dlugonski 2012 used a five-item Likert satisfaction scale and found that participants were most satisfied with the overall programme (mean \pm SD): 4.8 \pm 0.4, staff: 4.9 \pm 0.2 and pedometer: 4.7 \pm 0.6, but slightly less satisfied with the website: 4.1 \pm 0.9.

Huijgen 2008 used a six-item Visual Analogue Scale (VAS) to evaluate users' and therapists' satisfaction with the upper limb telerehabilitation intervention. Overall, both participants and therapists were satisfied with the intervention (over 55% in all six items). The authors found that both participants and therapists were less satisfied with the aesthetic aspect of the intervention and had difficulty in completing prescribed tasks.

No studies reported data on cost effectiveness, investment costs or resource utilisation. None of the included studies reported any serious adverse effects attributable to telerehabilitation. carer burden or social integration (in the form of return to work, study etc.) were not evaluated in any of the studies.

DISCUSSION

This review investigated the effectiveness of different forms of organised telerehabilitation in adults with multiple sclerosis (MS) on measures of activities, impairments and participation based on the International Classification of Functioning, Disability and Health (ICF) framework (WHO 2001), and also of the safety and cost effectiveness of these interventions. There was marked heterogeneity between the included trials in terms of characteristics, type and mode of delivery of the telerehabilitation interventions, measurement tools used (even for identical outcomes), treatment and control protocols and length of follow-up. We therefore performed a best-evidence synthesis using a qualitative analysis.

Summary of main results

This review of nine randomised controlled trials (RCTs) (one with two reports), involving 531 participants with MS (N = 277 participants in the intervention group) evaluated a wide variety of telerehabilitation interventions (see Table 2). All telerehabilitation interventions were complex, using more than one active rehabilitation component which differed in many aspects, including intervention goals, number and extent of the intervention components, duration and intensity, and mode of delivery. Control interventions also differed between studies ranging from 'usual care' or 'wait-list' to active intervention (such as hippotherapy, Frevel 2014). Most interventions included physical activity as one of the main intervention components, followed by education and behavioural training. The included trials were heterogeneous in terms of outcome measures used and study quality. Quantitative synthesis was therefore not possible. A qualitative synthesis of 'best evidence' for telerehabilitation interventions indicates *low level evidence* for:

- Short-term benefit in improving functional activities, such as physical activity, balance capacity and postural control compared with baseline, and some benefit in improving walking, physical activity;
- Short-term benefit in reducing and/or improving impairments, such as fatigue, and long-term benefits in improving symptoms such as fatigue, pain and insomnia;
- Longer-term improvement in participation, such as improving psychological outcomes and quality of life (QoL)

There is a 'very low' level of evidence for participants' and therapists' satisfaction with the telerehabilitation interventions.

The quality of evidence is further compromised by the limited number of studies, heterogeneity and the methodological weaknesses identified (underpowered with small sample sizes, high risk of bias, short follow-up periods, lack of rigorous methodology and different outcome measures) amongst the included trials.

Subgroup analysis for type of telerehabilitation intervention (unidisciplinary or multidisciplinary, or both), type of MS (relapsing

remitting, progressive), severity of MS (Expanded Disability Status Scale (EDSS) < 6; > 6) and duration of follow-up of participants (≤ 3 months; > 3 months) was not possible due to lack of data. There were no data for the cost effectiveness of telerehabilitation interventions, their impact on health service utilisation (hospitalisation or attendance/access to the health services) and carer burden or social integration (in the form of return to work, study etc.). There were limited data on process evaluation (satisfaction and acceptance of the telerehabilitation) and no reports of serious adverse effects attributable to telerehabilitation.

Overall completeness and applicability of evidence

Overall, this review indicates that telerehabilitation has some impact on improving function and symptoms (including cognitive function), but does not have an appreciable impact on disease-specific QoL in persons with MS (pwMS). There are no cost data or data on hospitalisation or access to other services. As aforementioned, there was marked variation between studies concerning the content and mode of delivery of the interventions. This highlights the diversity of programmes currently offered to pwMS.

Pooling data for meta-analyses to make meaningful statements for both primary and secondary outcomes was not possible. The generalisability and applicability of the results are limited, as most studies recruited participants from a single centre with strict inclusion and exclusion criteria. Moreover, generalisability of results to different countries and healthcare systems also seems limited, as the studies were conducted predominantly in the USA and Europe.

Quality of the evidence

In general, we rated the nine included studies (one with two reports) as of 'low' methodological quality due to substantial flaws in their methodological design with various biases observed. These included a lack of proper randomisation, problems with allocation concealment and a lack of blinding. Further, there was also insufficient information about these specific methodological issues, so that many domains of the 'Risk of bias' tables are rated as 'unclear' (see Figure 2 and Figure 3). All studies except one were single-centre trials, with fairly small participant numbers, with a concomitant risk of type I and II errors. The evidence is very heterogeneous, particularly in terms of interventions (technology employed, rehabilitation components within the intervention, duration and intensity of the intervention etc.), and diverse outcome measures used. The other methodological flaws include:

- High risk of selection bias, as only three studies (Finlayson 2011; Frevel 2014; Sandroff 2014) described allocation concealment
- Lack of description of the randomisation procedure, adequately reported in only three studies (Finlayson 2011; Frevel 2014; Paul 2014)
- High risk of performance bias due to non-blinding of the study participants and treating personnel; participants were blinded to group allocation in only one study (Finlayson 2011), but treating personnel were not blinded; and only one study took measures to blind outcome assessors (Gutiérrez 2013a)
- Most studies were underpowered with small sample sizes
- Lack of an intention-to-treat analysis protocol in most trials

- Lack of longer-term follow-up to detect the long-term effects of intervention; only three studies (one with two reports) followed the participants beyond three months (Egner 2003; Finlayson 2011; Pilutti 2014);
- Lack of control for participants' personal and other confounding factors, which influence patient-therapist interaction, compliance, and delivery of therapy, thus impacting on outcomes such as participant motivation and self efficacy, comorbidity and activity level outside of therapy programmes (not assessed in any of the studies).

Potential biases in the review process

We conducted the search in conjunction with the Trials Search Coordinator from the Cochrane Multiple Sclerosis and Rare Diseases of the Central Nervous System Working Group in the Cochrane MS Group Specialised Register using a broad search strategy. In order to avoid publication bias, we performed literature searches at three different time points. This process would have captured both published and ongoing trials coded as MS by the Cochrane MS Group. Two review authors further selected relevant articles from this extensive list independently and agreed on a final list of included studies by consensus between all four review authors. We applied no language restriction, although all the included trials were published in English. Overall, the review methodology is comprehensive, as described in the *Cochrane Handbook for Systematic Reviews of Interventions* (Higgins 2011). However, we recognise a number of limitations in the methodology of the review itself, and the completeness of the retrieved literature:

1. Four of the included studies in this review (Dlugonski 2012; Motl 2011; Pilutti 2014; Sandroff 2014) were conducted by the same group of authors in the same cohort of participants recruited from a single database, and using the same behavioural intervention (modified in recent publications). Hence, we cannot rule out overlapping of the participants amongst the studies.
2. We categorised outcomes according to the World Health Organization (WHO) ICF, which might have posed some methodological problems, since many of the outcome measures used in the included trials crossed the boundaries between the different levels of the ICF model. However, this model is widely used worldwide and helpful in clarifying the experience of people who live with long-term neurological conditions, such as MS (Khan 2007).
3. We cannot rule out some degree of selection bias from the literature search (Van Tulder 2003), given that the search strategy principally encompassed the cited literature, despite the extended range of terms for both MS and telerehabilitation that we used to capture the widest possible selection from the relevant literature.
4. We cannot rule out publication bias as we cannot exclude the possibility that there have been negative trials that have not reached the published literature (Egger 1998).
5. Reference bias (Goetzsche 1987) is possible, as we searched the bibliography lists of only relevant papers for other possible articles missed in our electronic searches.

We therefore welcome contact from any readers who are aware of important studies that would meet the criteria for this review, but have not so far been included.

Agreements and disagreements with other studies or reviews

To date, there has been no systematic review assessing the effectiveness of telerehabilitation in pwMS to guide treating clinicians or policy makers. Positive effects and successful implementation of telerehabilitation were reported in various neurological conditions including stroke (Johansson 2011; Legg 2004), Parkinson's disease (Giansanti 2008) and other non-neurological conditions such as musculoskeletal conditions (Russell 2011; Tousignant 2011), injuries (Bendixen 2008; Forducey 2003; Houlihan 2011) and chronic diseases (Steel 2011). We found one systematic review (Hailey 2011) (also published earlier as a health technology assessment, Hailey 2010), with some overlap with our results. That review considered the evidence of benefit from the use of telerehabilitation for various conditions, including neurological ones. The authors conducted comprehensive searches in multiple databases up to November 2009 and included two studies (one observational and one RCT) on telerehabilitation in the management of people with MS. That review provided simply an overview of studies on telerehabilitation for certain groups of conditions in terms of feasibility of interventions, the clinical significance of results, and a requirement for further data to establish the application as suitable for routine use. Consistent with the results of our review, the authors found inconsistent or insufficient evidence of benefit for telerehabilitation interventions and their impact on routine rehabilitation programmes.

AUTHORS' CONCLUSIONS

Implications for practice

Multiple sclerosis (MS) is a complex condition with different patterns of presentation and variable prognoses. The care needs in this population are complex due to cumulative effects of the impairments and disabilities, the 'wear and tear', and the impact of aging with a disability. Therefore, issues related to progressive disability, psychosocial adjustment and social re-integration progress over time need to be considered. These have implications for persons with MS (pwMS), their family/carers, treating clinicians and society as a whole, in terms of healthcare access, provision of services and financial burden (Beer 2012; Khan 2010a). Multidisciplinary rehabilitation is recommended and proven to be effective for pwMS, both in hospital and in communities, to maintain functional gains and social re-integration (participation) (Khan 2007). However, many pwMS are unable to access appropriate treatment due to limited mobility, fatigue and related issues, and limited access to services, and the costs and time associated with travel.

With advances in information and communication technology, new models of care such as telerehabilitation can be an alternative efficient and cost-effective method to deliver rehabilitation. The MS population is likely to be receptive to and benefit from this type of care model as most are young and have high rates of internet use (Motl 2011; NMSS 2007). Telerehabilitation is an alternative to traditional face-to-face interventions, providing equal access for individuals who are geographically remote and for those who are physically and economically disadvantaged, and can improve the quality of rehabilitation delivered by addressing associated issues of efficacy, problems of generalisation and increasing patient participation and satisfaction with treatment (Hailey 2011;

Kairy 2009; Rogante 2010). It can give healthcare providers an opportunity not only to evaluate the interventions previously prescribed, but also to monitor adverse events and identify areas in need of improvement by evaluating patients' progress (McCue 2010). Moreover, it provides an opportunity to optimise the timing, intensity and duration of therapy as required, which may not always be possible within the constraints of face-to-face treatment protocols and scheduling in current health systems (Hailey 2011; Steel 2011). MS is a complex and challenging condition requiring individualised and integrated multidisciplinary care. The range of telerehabilitation interventions and their intensity requirements can vary from person to person and are difficult to standardise. Various factors such as the patient's personal characteristics, their comorbidities, functional and coping abilities, family dynamics, and the healthcare system may impact patient outcomes (Khan 2010b). There is a paucity of information on the interaction of these factors on patient outcomes and very little is understood about the 'black box' of rehabilitation in the MS population (Khan 2010b).

This review highlights the lack of robust, methodologically-strong studies evaluating the effectiveness of telerehabilitation intervention in this population. Overall, the review found low quality evidence for a beneficial effect of telerehabilitation interventions on reducing short-term disability and impairments, such as fatigue. There was also low-quality of evidence suggesting some benefit in improving functional activities and impairments in the longer term, and improving psychological outcomes and quality of life (QoL). There are limited data on process evaluation (participants' and therapists' satisfaction) and, surprisingly, none of the studies addressed cost effectiveness.

Telerehabilitation has a major role in providing remote rehabilitation to people with chronic neurological conditions in future, and has potential to fill the existing service gap in the care of pwMS. However, the clinical applicability of the findings of this review and the effectiveness of telerehabilitation interventions need to be confirmed in future research.

Implications for research

This review found various limitations and gaps in knowledge, which could suggest directions for future research. These include, but are not limited to:

- More methodologically robust studies, e.g. randomised controlled trials (RCTs) comparing different models and intensity of telerehabilitation
- Large-scale systematic and 'practice-based trials' in which data are routinely gathered without disrupting the natural milieu of treatment to provide valuable information about outcomes in real-life clinical settings
- Use of more sensitive and appropriate validated outcome measures that are important for patients and their representatives and that focus on impairments, activity limitations and restriction in participation
- Longitudinal data in the MS population to ascertain long-term care needs
- More research about patient and carer perspectives and their involvement in telerehabilitation
- Research about specific telerehabilitation modalities and interventions in MS to improve evidence-based practices
- Cost effectiveness of telerehabilitation

- More emphasis on participatory domains (cognitive outcomes and quality of life (QoL)) in MS for impact on societal integration

Future studies in telerehabilitation should focus on improving the methodological and scientific rigour of clinical trials, with larger sample sizes and with longer-term follow-up. Further, active clinician involvement is needed to build evidence in this area for everyday clinical practice.

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* Indicates the major publication for the study

CHARACTERISTICS OF STUDIES

Characteristics of included studies [ordered by study ID]

Dlugonski 2012

Methods	RCT, parallel group with wait-list controls; USA
	Study period: one month period of July 2010
	Funding source: not mentioned
	Declaration of interest: not mentioned

Dlugonski 2012 (Continued)

Participants	<p>N = 45: treatment group = 22 and control = 23</p> <p><u>Inclusion:</u> Diagnosis of relapsing-remitting MS (RRMS); relapse-free in the past 30 days; Internet access; willingness to complete questionnaires; wear pedometer during intervention period; being non-active, defined as engaging in regular activity (30 minutes accumulated/day) on ≤ 2 days of the week during previous 6 months; ability to ambulate with or without assistance (i.e., walking with or without a cane/walker, but not a wheelchair or scooter); free of contraindication for physical therapy (e.g., no underlying cardiovascular disease); physician approval for beginning a physical activity programme</p> <p><u>Exclusion:</u> not specified</p> <p><u>Demographic characteristics:</u></p> <p>Mean age 46.6 years (SD: 9.7 years), 86.7% women, mean time since diagnosis 9.4 years (SD: 7.8 years), 64.4% had at least college degree, 95.6% white, 62.2% employed and 73.3% married</p>
Interventions	<p>(similar to Motl 2011)</p> <p><u>Treatment group:</u> Internet-delivered and social cognitive theory (self efficacy, outcome expectations, impediments, and goal setting) based behavioural intervention supplemented with video coaching for 12 weeks, which included text-based content supplemented by video and portable document format (PDF) files (i.e. multimedia). The intervention consisted of 4 essential modules: Getting Started (benefits of physical activity and information for becoming more physically active), Planning for Success (goal setting and feedback, outcome expectations, and self efficacy), Beating the Odds (barriers and strategies of overcoming barriers, and social support), and Sticking with It (maintaining an active lifestyle and physical activity relapse prevention), with 10 total Chapters. This was further supported by automated e-mail announcements about new information, updates, and changes on the web-site</p> <p>Additionally, 7 one-on-one web-based video coaching interactive sessions (5 - 10 minutes) using web-cam were conducted (4 in the first month, 2 in second month and 1 in third month), by an experienced doctoral student. The coaching sessions included discussions about progress towards goal achievements, content of website and adverse events</p> <p>For goal-setting and self-monitoring purposes a pedometer, log book to record steps and computer programme "Goal tracker" to upload weekly steps counts onto the website were provided</p> <p><u>Control group:</u> wait-list participants, who received the intervention materials after study completion</p>
Outcomes	<p><u>Primary outcome:</u> Physical activity: GLTEQ</p> <p><u>Secondary outcome:</u> Walking mobility: MSWS-12; QoL: MSIS-29; disease severity: PDDS; participant satisfaction (Process evaluation questionnaire)</p> <p>Assessment time points: Baseline, post-intervention (12 weeks) and 3 months</p>
Notes	<p>This study follows an earlier study (see below Motl 2011) and evaluated the same cohort of participants from a single database for similar intervention</p>
Risk of bias	
Bias	Authors' judgement Support for judgement
Random sequence generation (selection bias)	<p>Unclear risk</p> <p>Participants were paired based on their baseline level of activity (GLTEQ) and neurologic disability (PDDS) score by the authors, then randomised using a random number table</p>
Allocation concealment (selection bias)	<p>High risk</p> <p>Not reported, as randomisation was performed pairwise, allocation concealment was unlikely</p>

Dlugonski 2012 (Continued)

Blinding of participants and personnel (performance bias) All outcomes	High risk	No blinding of participants and treating personnel
Blinding of outcome assessment (detection bias) All outcomes	High risk	No blinding of outcome assessors
Incomplete outcome data (attrition bias) All outcomes	Low risk	Overall, only 1 participant from control group dropped out. ITT analysis performed
Selective reporting (reporting bias)	Low risk	All prespecified (primary and secondary) outcomes reported
Other bias	Unclear risk	Selective participants: recruitment occurred through a database of self-volunteering persons for research

Egner 2003

Methods	<p>RCT, 3 parallel groups; USA</p> <p>Study period: not mentioned</p> <p>Funding source: grant from the Centers for Disease Control and Prevention, National Center on Birth Defects and Developmental Disabilities, USA</p> <p>Declaration of interest: not mentioned</p>
Participants	<p>N = 27: Group 1 (video) = 9; Group 2 (telephone) = 11 and Group 3 (standard care) = 7</p> <p><u>Inclusion:</u> diagnosis of MS; experience of a recent functional setback in the disease process, such as a severe exacerbating episode or an increase or start of chemotherapy treatment; EDSS score ≥ 7</p> <p><u>Exclusion:</u> not specified</p> <p><u>Demographic characteristics:</u></p> <p>Mean age 46.0 years (SD: 9.0 years), 63% women, 44% married, 37% African –Americans and mean EDSS score of 7.8 (SD 0.6)</p>
Interventions	<p><u>Treatment group (Groups 1 and 2):</u> structured in-home education and counselling session delivered via telephone or video by a rehabilitation nurse, which included individual rehabilitation education sessions (structured review of skin care, nutrition, bowel and bladder routines, psychosocial issues and any equipment needs, and referrals to mental health counsellors, physical therapists, or other health professionals as needed. The same protocol was followed for the video and telephone groups with video group trained in the use of the Plain Old Telephone System (POTS) units in their home which provided image and sound</p> <p>Sessions: 30 - 40 minutes, weekly for a period of 5 weeks, then once every 2 weeks for 1 month.</p> <p><u>Control group:</u> usual care with regular follow-up offered by the rehabilitation facility</p>
Outcomes	<p><u>Primary outcome:</u> Fatigue: FSS; HRQOL: QWB; Depression: CES-D</p> <p><u>Secondary outcome:</u> none</p> <p>Assessment time points: Baseline, 5 weeks during intervention, post-intervention (9 weeks) and every month for 24 months</p>

Egner 2003 (Continued)

Notes

This study was part of a larger study of the impact of a telerehabilitation intervention on people with severe mobility impairment, with people with spinal cord injuries and the prevention of pressure sores as the primary group of interest of the project

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Unclear risk	Participants were randomly assigned to 1 of 3 intervention groups: video, telephone, or standard care. Further details not provided
Allocation concealment (selection bias)	Unclear risk	Not reported
Blinding of participants and personnel (performance bias) All outcomes	High risk	No blinding of participants and treating personnel
Blinding of outcome assessment (detection bias) All outcomes	High risk	No blinding of outcome assessors
Incomplete outcome data (attrition bias) All outcomes	Low risk	No drop-outs in either group
Selective reporting (reporting bias)	Low risk	All prespecified (primary and secondary) outcomes reported
Other bias	Unclear risk	Participant recruitment process and methodology not described in detail No power calculation for the study Small sample size with unbalanced allocation of participants to groups ITT analysis not performed

Finlayson 2011

Methods	<p>RCT, 2-group time series design with a wait-list control group; USA</p> <p>Study period: November 2007 to April 2009</p> <p>Funding source: Field-Initiated Research Grant, National Institute of Disability and Rehabilitation Research, USA</p> <p>Declaration of interest: authors declared no conflict of interest</p>
Participants	<p>N = 190: treatment group = 94 and control group = 96</p> <p><u>Inclusion:</u> living within the state of Illinois; diagnosis of MS; ≥ 18 years; functional English literacy; Fatigue Severity Scale (FSS) score ≥ 4 (i.e. moderate to severe fatigue); weighted score of at least 12 on the short version of the Blessed Orientation Memory Concentration test.</p> <p><u>Exclusion:</u> not provided</p> <p><u>Demographic characteristics:</u></p>

Finlayson 2011 (Continued)

Mean age 56 yrs (SD 9), 79% women, mean disease duration 15 yrs (SD 9 yrs), 88% white, 52% RRMS; 37% employed; 98% with education > 12 years

Interventions	<p><u>Treatment group</u>: a 6-week group-based, teleconference-delivered (70-minute) fatigue management programme, facilitated by a licensed OT</p> <p><u>Control group</u>: wait-list control group receiving treatment after 8 - 12 weeks</p>
Outcomes	<p><u>Primary outcome</u>: fatigue impact: FIS, fatigue severity: FSS; HRQoL:SF-36</p> <p><u>Secondary outcome</u>: self efficacy: ECQ</p> <p>Assessment time points: Baseline, post-intervention (6 weeks) 3 months and 6 months</p>
Notes	No adverse events were identified during the trial

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Low risk	Participants' randomisation completed by the statistician using a random permuted block design with each block consisting 4 people
Allocation concealment (selection bias)	Low risk	Opaque envelopes were used and prepared in advance of recruitment. The envelopes were numbered sequentially and a statement indicating the allocation (immediate or wait-list) was placed in each envelope
Blinding of participants and personnel (performance bias) All outcomes	Unclear risk	Participants blinded to group allocation only and treating personnel not blinded
Blinding of outcome assessment (detection bias) All outcomes	High risk	No blinding of outcome assessors
Incomplete outcome data (attrition bias) All outcomes	High risk	Overall 39 participants (20.5%) drop-out (17 in intervention, 22 in control group)
Selective reporting (reporting bias)	Low risk	All prespecified (primary and secondary) outcomes reported
Other bias	Unclear risk	ITT analysis performed for effectiveness analysis

Frevel 2014

Methods	<p>RCT, parallel group; Germany</p> <p>Study period: not mentioned</p> <p>Funding source: not mentioned</p> <p>Declaration of interest: not mentioned</p>
Participants	<p>N = 18: treatment group = 9 and control = 9</p> <p><u>Inclusion</u>: Definite MS diagnosis according to McDonald's criteria, EDSS 2-6, ability to stand with or without an assistive device for 1 minute, age 18 - 60 years, clinical stability for last 4 weeks</p>

Frevel 2014 (Continued)

Exclusion: clinically relevant internal or orthopaedic diseases unrelated to MS, an allergy or aversions to horses or previous experience with hippotherapy or therapeutic ridings (since diagnosis of MS)

Demographic characteristics:

Mean age 45.5 years (range 32 - 57), mean EDSS 3.8 (range 2 - 6), mean disease duration 19.0 (range 1 - 35), RRMS 67%

Interventions	<u>Treatment group:</u> Internet-based home training: balance, postural control exercises and strength training for main group of muscles of the lower extremities, trunk and shoulder griddle. Participant provided feedback (Borg scale) to the therapist, which provided further feedback after each sessions (duration 2 training sessions (45 minutes)/week for 12 weeks). Further, participants had an informative supervised meeting and received instructions and software prior	
	<u>Control group:</u> hippotherapy twice per week/ 20 – 30 minutes under supervision of riding therapist for 12 weeks	
Outcomes	<u>Primary Outcomes:</u> Balance: BBS, DGI	
	<u>Secondary outcomes:</u> Isometric muscle strength of knee and trunk; TUG; 2MWT; HAQUAMS, FSS, MFIS	
	Assessment time points: Baseline and post intervention (12 weeks)	
Notes	No report of adverse events	
<i>Risk of bias</i>		
Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Low risk	Randomised by simple allocation by drawing lots of preshuffled opaque envelopes
Allocation concealment (selection bias)	Low risk	Sealed opaque envelopes containing an identifier were used
Blinding of participants and personnel (performance bias) All outcomes	High risk	No blinding of participants and treating personnel
Blinding of outcome assessment (detection bias) All outcomes	High risk	No blinding of outcome assessors
Incomplete outcome data (attrition bias) All outcomes	Low risk	Overall, 2 participants in treatment group dropped out (11%)
Selective reporting (reporting bias)	Low risk	All prespecified (primary and secondary) outcomes reported
Other bias	Unclear risk	No power calculations for the study
		No ITT analysis
		Small sample size

Gutiérrez 2013a

Methods	<p>RCT, parallel group; Spain</p> <p>Study period: not mentioned</p> <p>Funding source: not mentioned</p> <p>Declaration of interest: authors declared no conflict of interest</p>
Participants	<p>Spain. N = 50: treatment group = 25 and control group = 25</p> <p><u>Inclusion:</u> Confirmed diagnosis of MS for > 2 years based on McDonald's criteria; age 20 - 60 years; medically stable during 6 months prior to baseline assessment; impaired balance demonstrated by MRI; EDSS score of 3 - 5; Hauser ambulatory index > 4, absence of cognitive impairment (MMSE \geq 24); no visual deficit; internet connection at home.</p> <p><u>Exclusion:</u> diagnosis with other disease or pathological condition that affects balance; had a relapse in the month prior to baseline or during the intervention process; received intravenous or oral steroid cycle prior to beginning the evaluation protocol and within 4-month duration of intervention</p> <p><u>Demographic characteristics:</u></p> <p>Treatment group: Mean age 39.7 years (SD 8.1), 54% women, mean disease duration 9.7 years (SD 6.8), EDSS score \geq 4: 83.6%, RR MS: 71.9%</p> <p>Control group: mean age 42.8 years (SD 7.4), 61% women, mean disease duration 10.9 years (SD 5.4), EDSS score \geq 4: 78.3%, RR MS: 65.2%</p>
Interventions	<p><u>Treatment group:</u> monitored virtual reality telerehabilitation programme via video-conference using the Xbox 360® and Kinect console, which included gaming protocol consisted of 3 games (Kinect Sports, Kinect Joy Ride, and Kinect Adventures).proposing activities that involve integrating proprioceptive, visual, and vestibular sensory information. Responses directed to the maintenance of balance and postural stability are triggered by the visual feedback that participants continuously receive in real time with regard to their position, performance type, and the movement direction that the task requires. The protocol proposed tasks such as throwing and hitting objects with one's hands and feet, hitting and receiving balls with different body parts, dodging objects, overcoming obstacles, imitating postures, or managing virtual elements that favour key aspects of postural control (e.g., girdle dissociation, alternating load distribution, changes in direction, multidirectional movement, reaction speed, hand-eye co-ordination, foot-eye co-ordination, and dexterity) in different positions across a stepwise gradient of difficulty. Experimental group attended 40 sessions, 4 sessions per week (20 minutes per session) at home</p> <p><u>Control group:</u> Ambulatory PT twice/week for 10 weeks (40 minutes per session) at rehab centre</p>
Outcomes	<p><u>Primary outcome:</u> Postural control : CDP; SOT; motor function: MCT</p> <p><u>Secondary outcome:</u> clinical outcomes: BBS, TS</p> <p>Assessment points: Baseline and post-intervention (10 weeks)</p>
Notes	<p>No report of adverse events</p> <p>Short-term follow-up</p> <p>Same study published in different journals by the same authors (Gutiérrez 2013b)</p>

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	High risk	Participants allocated to treatment or control groups based on the specific criteria. Only after screening for the treatment group, remaining participants were randomly distributed into 2 groups using computer software. Further,

Gutiérrez 2013a (Continued)

		2 participants were added to the treatment group due to availability of the equipment
Allocation concealment (selection bias)	High risk	No allocation concealment
Blinding of participants and personnel (performance bias) All outcomes	High risk	No blinding of participants and treating personnel
Blinding of outcome assessment (detection bias) All outcomes	Low risk	Outcome assessors were blinded
Incomplete outcome data (attrition bias) All outcomes	Low risk	3 drop-outs (1 in treatment group and 2 in control group)
Selective reporting (reporting bias)	Low risk	All prespecified (primary and secondary) outcomes reported
Other bias	High risk	No power calculation No ITT analysis Small sample size

Huijgen 2008

Methods	<p>RCT, parallel group, multicentred; Italy, Spain and Belgium</p> <p>Study period: October 2005 to January 2007</p> <p>Funding source: study was part of a project supported by European Union</p> <p>Declaration of interest: not mentioned</p>
Participants	<p>N = 81 (Stroke = 16, TBI = 30, MS = 35): treatment group = 55 (MS = 24) and control = 26 (MS = 11)</p> <p><u>Inclusion:</u> age > 18 years; confirmed diagnosis of MS, stroke or TBI; Nine Hole Peg Test > 25 sec and ability to move at least 1 peg in 180 sec; sufficient autonomous functioning; Internet connection or telephone line and reachable Internet provider; stable clinical status and living at home</p> <p><u>Exclusion:</u> disturbed upper limb function not related to MS, stroke or TBI; serious cognitive and/or behavioural problems; serious emotional problems; major visual problems; communication problems; medical complications; other problems possibly contraindicating autonomous exercise at home</p> <p><u>Demographic characteristics:</u></p> <p>Intervention group: mean age: 47 years (SD 18) (MS 48 years (SD 12)), 71% men (MS 46% men), mean disease duration 9.7 years (SD 7.8 years) (MS 15.1 years (SD 8.6));</p> <p>Control group: mean age: 50 years (SD 18) (MS 51 years (SD 14)), 69% men (MS 64% men), mean disease duration 10.2 years (SD 7.6 years) (MS 15.6 years (SD 7.8))</p>
Interventions	<p><u>Treatment group:</u> 1 month of usual care followed by the Home Care Activity Desk (HCAD) – a telerehabilitation intervention for arm/hand function at home which consisted a set of exercises for correct functional activity of the upper limb such as reaching, grasping, lateral pinch, pinch grip, holding, manipulation and finger dexterity; and additional features for videoconferencing and recording. HCAD sys-</p>

Huijgen 2008 (Continued)

tem comprised a hospital-based server and portable unit installed at participant's home. At least 1 session (30 minutes)/day for 5 days per week for 1 month

Control group: Usual care and generic exercises prescribed by their physicians

Outcomes	<u>Primary outcome:</u> Upper limb function : ARAT; NHPT <u>Secondary outcome:</u> participant satisfaction (VAS)
Notes	No report of adverse events Heterogeneous in approach and intensity for control group activities Higher percentage of men in the control group

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Unclear risk	Participants randomly allocated to treatment or control group, in such way to fit the clinical practice in a 2:1 ratio
Allocation concealment (selection bias)	High risk	No allocation concealment
Blinding of participants and personnel (performance bias) All outcomes	High risk	No blinding of participants and treating personnel
Blinding of outcome assessment (detection bias) All outcomes	High risk	No blinding of outcome assessors
Incomplete outcome data (attrition bias) All outcomes	Unclear risk	Overall 11 participants (14%) were lost to follow-up (7 in intervention, 4 in control group). Percentage of drop-outs reported but not time points
Selective reporting (reporting bias)	Low risk	All prespecified (primary and secondary) outcomes reported
Other bias	Unclear risk	Study was underpowered

Motl 2011

Methods	RCT, parallel group, with wait-list control; USA Study period: not mentioned Funding source: none Declaration of interest: authors declared no conflict of interest
Participants	N = 54: treatment group = 27 and control = 27 <u>Inclusion:</u> Definite diagnosis of RRMS; independently ambulatory or ambulatory with single-point assistance (i.e. cane); relapse-free in the past 30 days; Internet access; willingness to complete the questionnaires and undergo randomisations; being non-active defined as not engaging in regular physical activity (30 minutes accumulated per day) on more than 2 days of the week during the previous 6 months;

Motl 2011 (Continued)

free of contraindications for physical activity (e.g. no underlying cardiovascular disease); and physician approval for beginning a physical activity programme

Exclusion: not specified

Demographic characteristics:

Intervention group: mean age:46.1 years (SD 10.4), 90% women; mean disease duration: 8.1 years (SD 6.5); mean Determined Disease Steps Scale score (disease severity): 2.0 (SD 1.8)

Control group: mean age 45.6 (SD 9.2), 88% women, mean disease duration: 7.3 (SD 6.2), mean Determined Disease Steps Scale score (disease severity): 2.1 (1.9)

Interventions	<p><u>Treatment group:</u> Internet intervention based on social cognitive theory (self efficacy, outcome expectations, impediments, and goal setting), which included text-based content supplemented by video and portable document format (PDF) files (i.e. multimedia). It consisted of 4 essential modules: Getting Started (benefits of physical activity and information for becoming more physically active), Planning for Success (goal setting and feedback, outcome expectations, and self efficacy), Beating the Odds (barriers and strategies of overcoming barriers, and social support), and Sticking with It (maintaining an active lifestyle and physical activity relapse prevention), with 10 total Chapters. Additionally, interactive sessions twice per week were conducted, which included an ongoing participant forum for discussions of physical activity behaviour change, and a toll-free telephone line and a study e-mail address for supporting the website. This was further supported by automated e-mail announcements about new information, updates, and changes on the website</p> <p><u>Control group:</u> wait-list participants, who received the intervention materials after study completion</p>
Outcomes	<p>Measured at baseline, immediately post-treatment (12 weeks after start of intervention)</p> <p><u>Primary outcome:</u> Physical activity: GLTEQ; Self efficacy: EXSE; Outcome expectations: MOEES; Functional limitations: - Functional Limitations component of the abbreviated LL-FDI; Goal setting: EGS</p> <p><u>Secondary outcome:</u> Disease severity: PDDS</p> <p>Assessment time points: Baseline and post-intervention (1 month)</p>
Notes	No report of adverse events

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Unclear risk	Participants were initially paired on physical activity and neurological disability levels by 2 authors and then members of the pairs were randomly assigned into intervention or wait-list control conditions
Allocation concealment (selection bias)	High risk	No allocation concealment
Blinding of participants and personnel (performance bias) All outcomes	High risk	No blinding of participants and treating personnel
Blinding of outcome assessment (detection bias) All outcomes	High risk	No blinding of outcome assessors
Incomplete outcome data (attrition bias) All outcomes	Unclear risk	Overall 10 participants (15%) dropped out (6 in intervention, 4 in control group). Percentage of drop-outs reported but not time points

Motl 2011 (Continued)

Selective reporting (reporting bias)	Low risk	All prespecified (primary and secondary) outcomes reported
Other bias	Low risk	None

Paul 2014

Methods	<p>RCT, parallel group; Scotland, UK</p> <p>Study period: not mentioned</p> <p>Funding source: grant, the Chief of Scientist Office, Scotland</p> <p>Declaration of interest: authors declared no conflict of interest</p>
Participants	<p>N = 30: treatment group = 5 and control = 15</p> <p><u>Inclusion:</u> Confirmed diagnosis of MS, EDSS: 5 - 6, stable drug therapy for 30 days, no relapses in the previous 3 months, no significant comorbidities (such as co-existing cardiac or pulmonary condition), have access to the Internet via personal or tablet computer</p> <p>Further inclusion in the treatment group if participants did not receive conventional physiotherapy treatment based on at least 1 the following criteria: (a) time on the waiting list; (b) limited geographic accessibility; (c) unable to reconcile working hours and therapy schedule; or d) dependent on others to arrive at the treatment centre</p> <p><u>Exclusion:</u> not specified</p> <p><u>Demographic characteristics:</u></p> <p>Treatment group: Mean age 50.8 years (SD 7.4), 80% women; mean disease duration 12.5 years (SD 7.1), mean EDSS 6.0 (SD 0.5)</p> <p>Control group: Mean age 52.5 years (SD 14.3), 80% women; mean disease duration 12.8 years (SD 10.9), mean EDSS 5.8 (SD 0.5)</p>
Interventions	<p><u>Treatment group:</u> 12 weeks of individualised web-based physiotherapy completed twice per week. The website consisted of a home page, exercise pages and advice section. Each exercise page contained a video and text explaining the exercise, an audio description of the exercise and a timer. The catalogue of exercises consisted of: cardiovascular, strengthening and balance exercises, each at 4 levels of difficulty, as well as warm-up and cool-down exercises and stretches</p> <p><u>Control group:</u> usual care</p>
Outcomes	<p><u>Primary outcomes:</u> 25 Foot Walk Test</p> <p><u>Secondary outcomes:</u> BBS, TUG, MSIS, LMSQOLS, MS-Related Symptom Checklist, HADS, feasibility and satisfaction with the programme</p> <p>Assessment points: Baseline and post-intervention (12 weeks)</p>
Notes	<p>No report of adverse events</p> <p>Short-term follow-up</p>

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Low risk	Randomisation performed using a series of random numbers, generated in Microsoft Excel. Recruited participants were allocated consecutive numbers,

Paul 2014 (Continued)

		where even numbers represented the intervention group and odd numbers the control group
Allocation concealment (selection bias)	High risk	No allocation concealment
Blinding of participants and personnel (performance bias) All outcomes	High risk	No blinding of participants and treating personnel
Blinding of outcome assessment (detection bias) All outcomes	High risk	No blinding of outcome assessors
Incomplete outcome data (attrition bias) All outcomes	Low risk	Overall, 1 participant dropped out from control group
Selective reporting (reporting bias)	Low risk	All prespecified (primary and secondary) outcomes reported
Other bias	Unclear risk	Underpowered study No ITT analysis Small sample size

Pilutti 2014

Methods	<p>RCT, parallel group with wait-list controls, USA</p> <p>Study period: not mentioned</p> <p>Funding source: various grant from the National Multiple Sclerosis Society, USA; the Multiple Sclerosis Society of Canada and the Multiple Sclerosis International Federation</p> <p>Declaration of interest: authors declared no conflict of interest</p>
Participants	<p>N = 82: treatment group = 41 and control = 41</p> <p><u>Inclusion:</u> 18 – 64 years; definite diagnosis of MS based on physician verification; relapse-free for the past 30 days; Internet access; and ability to walk with or without an assistive device; physician's approval for participation; willing and able to travel to the research site; have minimal risk for engaging in physical activity (i.e. reported 'yes' to fewer than 2 questions on the PARQ)</p> <p><u>Exclusion:</u> participants who self-reported accumulating ≥ 30 minutes of moderate-to-vigorous physical activity per day on ≥ 2 days/week.</p> <p><u>Demographic characteristics:</u></p> <p>Treatment group: Mean age 48.4 years (SD: 9.1 years), 73.2% women, mean time since diagnosis 10.6 years (SD: 7.1 years), RRMS 75.6%, PDSS: median 2.0 (IQR 4, 0)</p> <p>Control group: Mean age 49.5 years (SD: 9.2 years), 78% women, mean time since diagnosis 13.0 years (SD: 9.1 years), RRMS 83%, PDSS: median 3.0 (IQR 3, 0)</p>
Interventions	<p><u>Treatment group:</u> same as in Dlugonski 2012, Motl 2011 (see above). In addition, participant wore a Yamax SW-401 Digiwalker pedometer, completed a log book and used Goal Tracker software, and received a web-cam, and website information. Participants participated in 15 scheduled one-on-one video coaching sessions for 6 months.</p>

Pilutti 2014 (Continued)

Control group: wait-list participants, who received the intervention materials after study completion.

Outcomes	<p><u>Primary outcome:</u> Physical activity: GLTEQ; fatigue: FSS, MFIS; depression and anxiety: HADS; pain: MPQ; sleep: PSQI; HRQoL: MSIS-29, Cognitive processing speed: SDMT</p> <p><u>Secondary outcome:</u> disease severity: PDDS</p> <p>Assessment time points: baseline and post-intervention (6 months)</p>
Notes	<p>This RCT was considered the primary study, whose results were described in 2 different articles reporting different outcomes (Sandroff 2014).</p> <p>This study is part of a series of studies conducted earlier (Dlugonski 2012 and Motl 2011).</p>

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Unclear risk	After baseline testing, participants were grouped into matched pairs based on step counts from the accelerometer and level of disability, and then randomly assigned to either the intervention or wait-list control condition using a random numbers sequence
Allocation concealment (selection bias)	High risk	Not reported
Blinding of participants and personnel (performance bias) All outcomes	High risk	No blinding of participants and treating personnel
Blinding of outcome assessment (detection bias) All outcomes	High risk	No blinding of outcome assessors
Incomplete outcome data (attrition bias) All outcomes	Low risk	Overall, 6 participants (7%) (4 from intervention and 2 from control group) dropped out
Selective reporting (reporting bias)	Low risk	All prespecified (primary and secondary) outcomes reported
Other bias	Unclear risk	<p>Selective participants: recruitment occurred through a database of self-volunteered persons for research</p> <p>No ITT analysis performed (analysis of completers only)</p> <p>USD 50 remuneration given to participants for completing each testing session</p>

ARAT: Action Research Arm Test; **BBS:** Berg Balance Scale; **CCT:** Controlled clinical trial; **CDP:** Computerized Dynamic Posturography; **CES:** Composite Equilibrium Score; **CES-D:** Center for Epidemiologic Studies Depression Scale; **CI:** Confidence interval; **DGI:** Dynamic gait Index; **EQQ:** Energy Conservation Questionnaire; **EDSS:** Expanded Disability Status Scale; **EGS:** Exercise Goal setting Scale; **ES:** Effect size; **EXSE:** Exercise Self-Efficacy Scale; **FIS:** Fatigue Impact Scale; **FSS:** Fatigue Severity Score; **GLTEQ:** Godin Leisure-Time Exercise Questionnaire; **HADS:** Hospital Anxiety and Depression Scale; **HAQUAMS:** Hamburg QoL Questionnaire in MS; **HCAD:** Home Care Activity Desk; **HRQoL:** Health related quality of life; **IPAQ:** International Physical Activity Questionnaire; **IQR:** inter quartile range; **ITT:** intention to treat; **LMSQOLS:** Leeds MS Quality of Life Scale; **LL-FDI:** Late-Life Function and Disability Instrument; **MCT:** Motor Control Test; **MOEES:** Multidimensional Outcomes Expectations for Exercise Scale; **MPQ:** McGill Pain Questionnaire; **MRI:** Magnetic Resonance Imaging; **MS:** Multiple Sclerosis; **MSIS-29:** MS Impact Scale; **MSWS-12:** MS Walking Scale – 12; **NHPT:** Nine Hole Peg Test; **PARQ:** Physical Activity Readiness Questionnaire; **PDDS:** Patient Determined Disease Steps; **PSQI:** Pittsburgh Sleep Quality Index; **QoL:** quality of life; **QWB:** Quality

of Well-Being Scale; **RCT**: randomised controlled trial; **RR**: Risk Ratio; **SD**: Standard deviation; **SDMT**: Symbol Digit Modalities Test; **SE**: Standard Error; **SF-36**: 36-Item Short Form Health Survey; **SOT**: Sensory organisation Test; **TBI**: traumatic brain injury; **TS**: Tinetti Scale; **TUG**: Timed Up and Go; **UK**: United Kingdom; **USA**: United States of America; **VAS**: Visual Analogue Scale; **2MWT**: 2 minute walk test; **6MWT**: 6 minute walk test; **25FWT**: 25 Foot Walk Test

Characteristics of excluded studies [ordered by study ID]

Study	Reason for exclusion
Amato 2014	Not intervention of interest (mental health care only)
Beckner 2010	Not intervention of interest (mental health care only)
Bombardier 2008	Not Intervention of interest (telephone counselling for health promotion)
Bombardier 2013	Not Intervention of interest (telephone counselling for major depression)
Cerasa 2013	Not intervention of interest (mental health care only)
Fischer 2013	Not intervention of interest (mental health care only)
Ghahari 2010	No subgroup analysis for MS participants
Miller 2011	Intervention with no rehabilitation objectives
Mohr 2000	Not intervention of interest (mental health care only)
Mohr 2005	Not intervention of interest (mental health care only)
Mohr 2007	Not intervention of interest (mental health care only)
Moss-Morris 2012	Not intervention of interest (mental health care only)
Solari 2004	Not intervention of interest (mental health care only)
Stuifbergen 2012	Not intervention of interest (mental health care only)
Wiles 2003	Intervention: no telerehabilitation
Zissman 2012	Not intervention of interest (medical care only)

ADDITIONAL TABLES

Table 1. List of outcome measures used in the included studies*

Outcome Measures
Function
Action Research Arm Test (ARAT)
Berg Balance Scale (BBS)
Computerized Dynamic Posturography (CDP)

Table 1. List of outcome measures used in the included studies* (Continued)

Composite Equilibrium Score (CES)
Dynamic gait Index (DGI)
Exercise Self-Efficacy Scale (EXCE)
Godin Leisure-Time Exercise Questionnaire (GLTEQ)
International Physical Activity Questionnaire (IPAQ)
Late-Life Function and Disability Instrument (LL-FDI)
Motor Control Test (MCT)
Multidimensional Outcomes Expectations for Exercise Scale (MOEES)
Multiple Sclerosis Walking Scale – 12 (MSWS-12)
Nine-Hole Peg Test (NHPT)
Physical Activity Readiness Questionnaire (PARQ)
Sensory organisation Test (SOT)
Six Meter Walk Test (6MWT)
Tinetti Scale (TS)
Timed Up and Go (TUG)
Two Meter Walk Test (2MWT)
Twenty-five Foot Walk Test (25-FWT)
Visual Preference Ratio (VPR)
<i>Impairment and symptoms</i>
Fatigue impact scale (FIS)
Fatigue severity scale (FSS)
Modified Fatigue impact scale (MFIS)
McGill Pain Questionnaire (MPQ)
MS related symptom check list
Pittsburgh Sleep Quality Index (PSQI)
<i>Participation</i>
<i>Quality of Life</i>
Hamburg Quality of Life Questionnaire in Multiple Sclerosis (HAQUAMAS)

Table 1. List of outcome measures used in the included studies* (Continued)

Leeds Multiple Sclerosis Quality of Life Scale (LMSQOL)
Multiple Sclerosis Impact Scale (MSIS-29)
Quality of Well-Being Scale (QWB)
36 item Short Form Health Survey Questionnaire (SF 36)
<i>Psychological</i>
Centre for Epidemiologic Studies Depression Scale (CES-D)
Hospital Anxiety and Depression Scale (HADS)
Symbol Digit Modalities Test (SDMT)
Other
Expanded Disability Status Scale (EDSS)
Energy Conservation Questionnaire (ECQ)
Exercise Goal setting Scale (EGS)
Muscle strength
Patient Determined Disease Steps (PDDS)
Self-Efficacy for Energy Conservation (SEEC)
Satisfaction with the intervention
Visual Analogue Scales (VAS)

*Outcome measures are categorised according to the International Classification of Functioning, Disability and Health (ICF, WHO 2001)

Table 2. Summary of telerehabilitation interventions in the included studies

Study	Telerehabilitation interventions			
	Contents	Settings	Technology	Duration/intensity
Dlugonski 2012	Same as Motl 2011 (see below)	Participants' home	Internet-delivered	12 weeks Same as Motl 2011 (see below)
Egner 2003	Structured in-home education and counselling session delivered by a rehabilitation nurse, which included individual rehabilitation education sessions	Participants' home	Telephone or video	30 to 40 minutes, weekly for 5 weeks, then once every 2 weeks for 1 month.
Finlayson 2011	Group-based fatigue management programme, facilitated by a licensed Occupational Therapist	Rehab centre	Teleconference	70-minute weekly for 6 weeks

Table 2. Summary of telerehabilitation interventions in the included studies (Continued)

Frevel 2014	Training programme: balance, postural control exercises and strength training with additional interactive sessions	Participants' home	Internet-delivered	2 training sessions/(45 minutes) weekly for 12 weeks
Gutiérrez 2013a	Monitored telerehabilitation programme, which included gaming protocol, proposing activities that involve integrating proprioceptive, visual, and vestibular sensory information. Experimental group attended at home	Participants' home	Virtual reality system via video-conference using the Xbox 360 and Kinect console	40 sessions, 4 sessions per week (20 minutes per session)
Huijgen 2008	Home Care Activity Desk (HCAD) – a telerehabilitation intervention for arm/hand function and additional features for videoconferencing and recording. HCAD system	Participants' home	Virtual telerehabilitation programme and video-conference, comprising a hospital-based server and portable unit installed at participant's home	1 month of usual care followed by HCAD- 1 session (30 minutes)/day for 5 days per week for 1 month
Motl 2011	Same as Dlugonski 2012 (see above)	Participants' home	Internet-delivered	Same as Dlugonski 2012 (see above)
Paul 2014	Individualised physiotherapy programme consisting of exercise page containing a video and text explaining the exercise, an audio description of the exercise and a timer	Participants' home	Internet-delivered	Twice per week for 12 weeks
Pilutti 2014	Same as in Motl 2011 (see above), in addition, participant wore a Yamax SW-401 Digiwalker pedometer, completed a log book and used Goal Tracker software, and received a webcam, and website information	Participants' home	Internet-delivered	15 scheduled one-on-one video coaching sessions for 6 months
Sandroff 2014	Same as in Motl 2011 , Pilutti 2014 (see above). In addition, website materials were delivered in a titrated manner over the 6-month period such that new content became available 7 times during the first 2-month period, 4 times during the second 2-month period, and twice during the final 2 months of the intervention.	Participants' home	Internet-delivered	Weekly one-on-one behavioural coaching sessions via Skype (15 scheduled sessions) for 6 months

Table 3. Summary of outcome assessed in the included studies

Study	Outcome assessed*			
	Function	Impairment	Participation	Others
Dlugonski 2012	GLTEQ, MSWS-12		MSIS-29	PDDS, SATISFACTION
Egner 2003		FSS	QWB, CES-D	
Finlayson 2011		FIS, FSS	SF-36	ECQ, PDDS

Table 3. Summary of outcome assessed in the included studies (Continued)

Frevel 2014	BBS, DGI, TUG, 2MWT	MFIS	HAQUAMAS	Muscle strength
Gutiérrez 2013a	SOT, MCT, BBS, TS			
Huijgen 2008	ARAT, NHPT			VAS satisfaction survey
Motl 2011	GLTEQ, LL-FDI, EXCE, MOEES			EGS, PDSS
Paul 2014	25 FWT, BBS, TUG	MS related symptom check list	MSIS, LMSQOL, HADS	
Pilutti 2014	GLTEQ	MFIS, FSS, MPQ, PSQI	MSIS-29, HADS	PDDS
Sandroff 2014	6MWT, IPAQ		SDMT	PDDS

*Categorised according to the International Classification of Functioning, Disability and Health (ICF, WHO 2001)

ARAT: Action Research Arm Test; **BBS:** Berg Balance Scale; **CDP:** Computerized Dynamic Posturography; **CES:** Composite Equilibrium Score; **CES-D:** Center for Epidemiologic Studies Depression Scale; **DGI:** Dynamic gait Index; **ECQ:** Energy Conservation Questionnaire; **EDSS:** Expanded Disability Status Scale; **EGS:** Exercise Goal setting Scale; **EXSE:** Exercise Self-Efficacy Scale; **FIS:** Fatigue Impact Scale; **FSS:** Fatigue Severity Score; **GLTEQ:** Godin Leisure-Time Exercise Questionnaire; **HADS:** Hospital Anxiety and Depression Scale; **HAQUAMS:** Hamburg Quality of Life Questionnaire in Multiple Sclerosis; **IPAQ:** International Physical Activity Questionnaire; **LMSQOLS:** Leeds Multiple Sclerosis Quality of Life Scale; **LL-FDI:** Late-Life Function and Disability Instrument; **MCT:** Motor Control Test; **MOEES:** Multidimensional Outcomes Expectations for Exercise Scale; **MPQ:** McGill Pain Questionnaire; **MSIS-29:** Multiple Sclerosis Impact Scale; **MSWS-12:** Multiple Sclerosis Walking Scale-12; **NHPT:** Nine Hole Peg Test; **PARQ:** Physical Activity Readiness Questionnaire; **PDDS:** Patient Determined Disease Steps; **PSQI:** Pittsburgh Sleep Quality Index; **QWB:** Quality of Well-Being Scale; **SDMT:** Symbol Digit Modalities Test; **SF-36:** 36-Item Short Form Health Survey; **SOT:** Sensory organisation Test; **TS:** Tinetti Scale; **TUG:** Timed Up and Go; **VAS:** Visual Analogue Scale; **6MWT:** 6 minute walk test; **25FWT:** 25 Foot Walk Test

APPENDICES

Appendix 1. Keywords

{telecommunications*} OR {telemedicine} OR {telehealth} OR {telehealthcare} OR {telecoaching} OR {e-health} OR {e-medicine} OR {mobile health} OR {information technology} OR {information communication technology} OR {internet} OR {web-based} OR {computer} OR {Software} OR {videoconferencing} OR {remote consultation} OR {remote sensing technology} OR {rehabilitation} OR {physiotherapy} OR {occupational therapy} OR {speech therapy} OR {dietician}

CONTRIBUTIONS OF AUTHORS

Fary Khan (FA), and Bhasker Amatya (BA) were involved in all aspects of the review. Jurg Kesselring (JK) provided valuable input into design of the review. Fary Khan, Bhasker Amatya, Mary Galea (MG) were responsible for all study selection, data extraction and methodological quality of included studies. M Galea and J Kesselring also provided valuable assistance with the Discussion. All review authors critically reviewed the manuscript and discussed data collection, results and conclusions.

DECLARATIONS OF INTEREST

The review authors are clinicians and researchers in the field of Physical and Medical Rehabilitation who wish to provide the best possible service to their patients.

Fary Khan: none known.

Bhasker Amatya: none known.

Jurg Kesselring: none known.

Mary Galea: none known.

SOURCES OF SUPPORT

Internal sources

- Department of Rehabilitation Medicine, Royal Melbourne Hospital, Australia.

External sources

- None, Other.

DIFFERENCES BETWEEN PROTOCOL AND REVIEW

We have included a 'Summary of findings' table in the review with the key outcomes identified categorised according to the WHO ICF framework, which the authors deemed to be the most relevant to decision-makers including patients, clinicians and policy makers.

We have clarified 'Types of interventions' in this review to include control conditions: "any type of traditional face-to face rehabilitation treatment in outpatient or day treatment settings".

We exclude studies if they investigated interventions related to: "telerehabilitation targeting mental health conditions or substance abuse"; "home care (or tele-home care) with no rehabilitation objectives"; "satisfaction with or acceptance of telerehabilitation technology" and "technical development or feasibility of telerehabilitation".

We modified 'Data extraction and management' for the review and added the following statement: "Data were extracted for intention-to-treat (ITT) analysis from each study and where ITT data were not available, 'on-treatment' data or the data of those who completed the trial were retrieved."

Based on the findings, we did not implement the planned methods as described in the protocol related to assessment of heterogeneity, assessment of reporting bias, and data synthesis.

INDEX TERMS

Medical Subject Headings (MeSH)

*Telemedicine; Multiple Sclerosis [*rehabilitation]; Randomized Controlled Trials as Topic; Treatment Outcome

MeSH check words

Adult; Humans; Middle Aged